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Kawamura et al.

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(54) **AGENT FOR IMPROVING LEARNING OR MEMORY**

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(58) **Field of Search** 514/250, 287

(56) **References Cited**

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Pavone et al., *Peptides*, vol. 11, No. 3, pp. 591-594 (1990).

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(57) **ABSTRACT**

Disclosed is an agent for improving learning and/or memory, which is useful for therapy of dementia accompanying disorder of memory due to a cerebrovascular disease, neurodegenerative disease such as Alzheimer's disease, endocrine disease, nutritional or metabolic disorder, infectious disease, drug addiction or the like. The agent for improving learning and/or memory according to the present invention comprises as an effective ingredient an isoquinoline derivative having a specific structure, such as (4aR, 12aR)-2-methyl-4a-(3-hydroxyphenyl)-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3-g]isoquinoline or a pharmaceutically acceptable salt thereof.

2 Claims, 3 Drawing Sheets

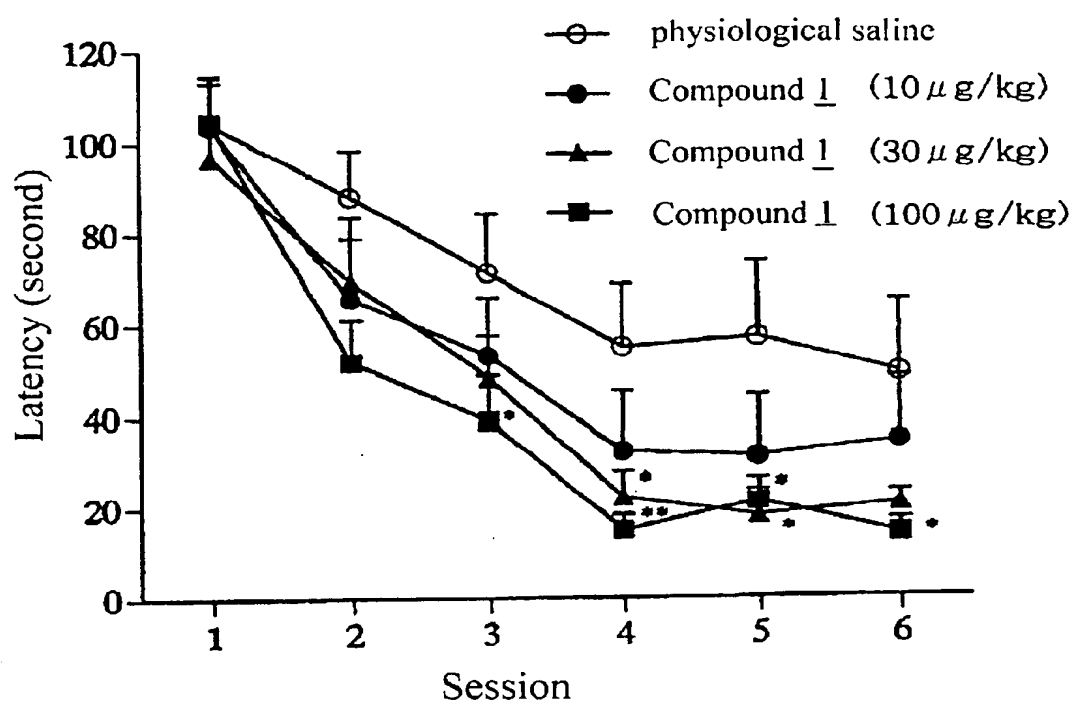


Fig. 1

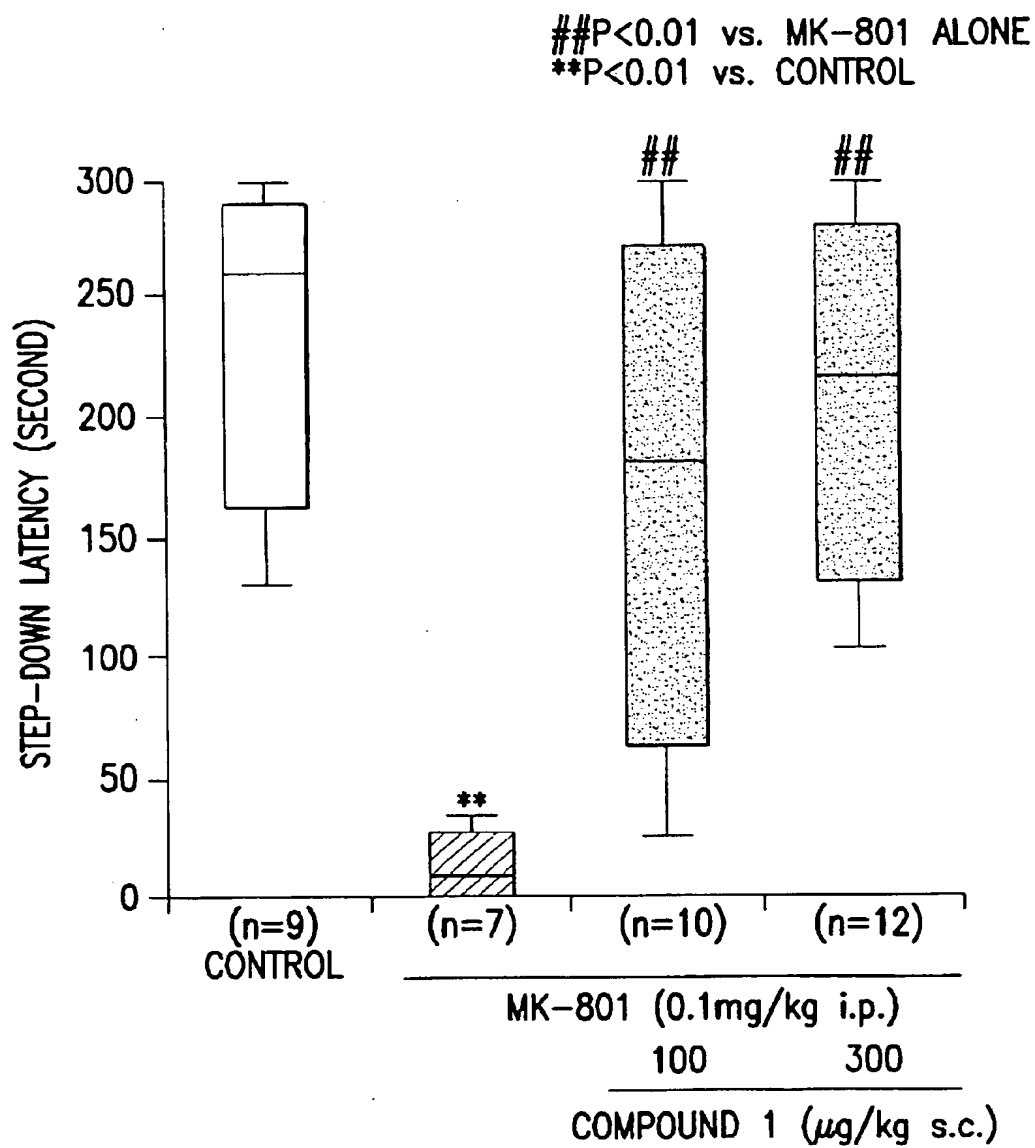


FIG.2

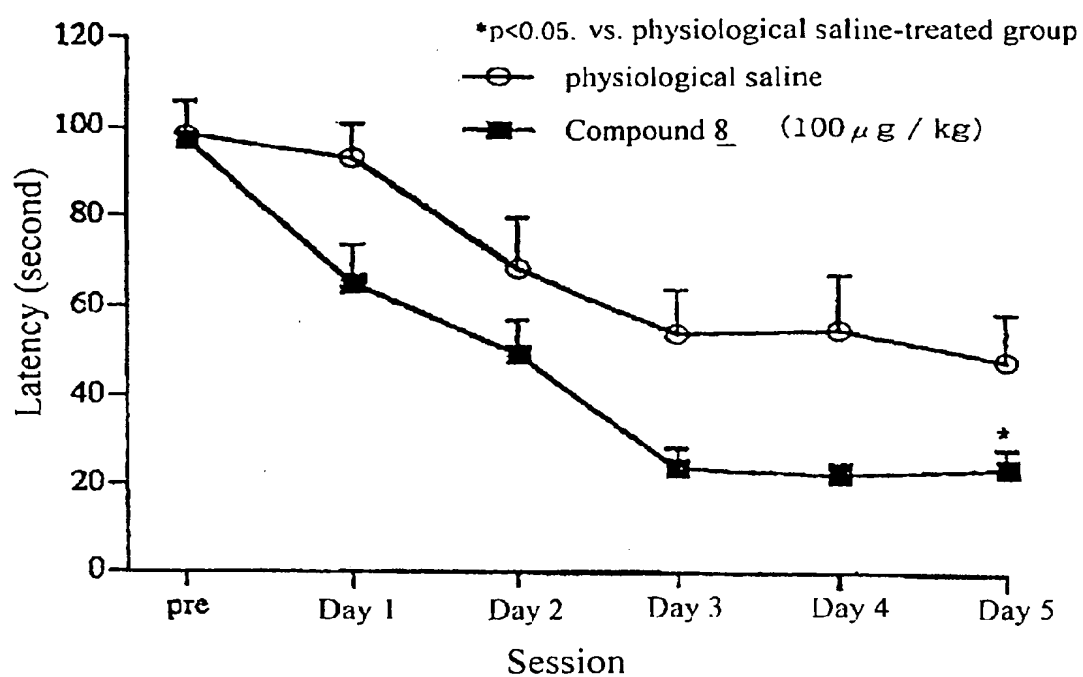


Fig. 3

AGENT FOR IMPROVING LEARNING OR MEMORY

This application is the national phase under 35 U.S.C. §371 of PCT International Application No. PCT/JP00/08847 which has an International filing date of Nov. 30, 2000, which designated the United States of America.

TECHNICAL FIELD

The present invention relates to an agent for improving learning and/or memory comprising as an effective ingredient a quinolinoisoquinoline derivative or a pharmaceutically acceptable acid addition salt thereof.

BACKGROUND ART

Learning means to acquire change in behavior, which continues for a relatively long time, which is caused by experience or practice, or the process for acquiring the change in behavior. Memory means to retain information for a certain time, which information is obtained through experience, and to retrieve the information as required. However, the definitions of these two concepts are not simple, and are not independent for each other but most of them overlap. Therefore, learning ability and memory are often measured by similar experiments in the field of behavioral pharmacology.

Learning includes the steps of encoding, storage, recognition and retrieval. Even if one of these steps is inhibited, disorder of memory occurs (Seiden, L. S. & Dykstra, L. A., Psychopharmacology, a biochemical and behavioral approach. Van Nostrand Reinhold Co., New York(1977)). A representative disease accompanying memory disorder and/or learning disability is dementia. The term "dementia" means the continuous state in which the intellectual ability is reduced, which intellectual ability had ever developed to the normal level. Symptoms of dementia include, in addition to memory disorder and/or learning disability, mood disorder, emotional disorder, intellectual disturbance and psychomotor disturbance. Improvement of memory disorder which likely to cause serious problems in social life is an indispensable action of anti-dementia drugs.

In the brains of patients suffering from senile dementia or Alzheimer's disease, remarkable reduction in neurotransmitters and biosynthesis enzymes thereof is observed. Therefore, therapy by drugs such as dopamine, noradrenalin, serotonin, acetylcholine and GABA, which act on the transmission process through neurotransmitters is drawing attention. Since it is known that the hypofunction of acetylcholine system is prominent in brains of patients suffering from dementia, the current mainstream of development of therapeutic method for dementia is the development of drugs targeting the activation of acetylcholine nervous system. An anti-dementia drug, tacrine, which has obtained approval, is an acetylcholinesterase inhibitor, and it has been confirmed that improvement of intellectual function to a certain degree is observed in about half of the cases in which the drug is administered. However, this drug has a problem in the hepatic toxicity and choline-related side effects. With Aricept effective for Alzheimer's disease through the similar mechanism, improvement is observed in about half cases for patients suffering from the dementia in light to medium degree.

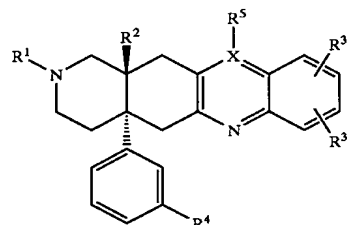
On the other hand, references disclosing quinolinoisoquinoline derivatives include Japanese Laid-open Patent Application (Kokai) No. 4-275288, WO93/01186 and WO99/02157. These patent literatures disclose the uses of

the derivatives as immunosuppressive agents, analgesics and antitussives. However, these references are totally silent about improvement of learning or memory.

DISCLOSURE OF THE INVENTION

The present inventors intensively studied to discover that specific isoquinoline derivatives exhibit excellent effect for improving learning and/or memory, thereby completing the present invention.

That is, the present invention provides an agent for improving learning and/or memory comprising as an effective ingredient an isoquinoline derivative of the Formula (I):



(I)

{wherein R¹ represents hydrogen, C₁-C₅ alkyl, C₄-C₇ cycloalkylalkyl, C₅-C₇ cycloalkenylalkyl, C₇-C₁₄ aralkyl, C₄-C₅ transalkenyl, allyl, furanyl-2-ylalkyl, thienyl-2-ylalkyl, C₁-C₅ alkanoyl, benzoyl, vinyloxy carbonyl, trichloroethoxycarbonyl, benzyloxy carbonyl or C₈-C₁₄ arylalkanoyle; R² represents hydrogen or OR⁶ (wherein R⁶ represents hydrogen, C₁-C₅ alkyl or C₁-C₅ alkanoyl); R³ and R³' independently represent C₁-C₅ alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxycarbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino, or C₁-C₃ alkylamino; R⁴ represents hydrogen, hydroxy, C₁-C₃ alkoxy, benzyl, or C₁-C₅ alkanoyl or halogen; X represents nitrogen or carbon; R⁵ exists only when X is carbon, and represents C₁-C₅ alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxycarbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino}

or a pharmaceutically acceptable salt thereof. The present invention also provides a use of said isoquinoline derivative represented by the above-described Formula (I) or the pharmaceutically acceptable salt thereof for the preparation of an agent for improving learning and/or memory. The present invention further provides a method for improving learning and/or memory comprising administering an effective amount of the isoquinoline derivative represented by the above-described Formula (I) or the pharmaceutically acceptable salt thereof.

By the present invention, an agent for improving learning and/or memory was provided, which is useful for therapy of dementia accompanying memory disorder due to a cerebrovascular disease, neurodegenerative disease such as Alzheimer's disease, endocrine disease, nutritional or metabolic disorder, infectious disease, drug addiction or the like.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the learning process of the rats to which Compound 1 that is the agent for improving learning and/or memory according to the present invention, in comparison with the learning process of the rats to which saline was administered.

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FIG. 2 shows the Step-Down latency of the group of mice to which MK-801 that is a compound inducing learning disability and memory disorder was administered and then Compound 1 which is the agent for improving learning and/or memory according to the present invention was administered, in comparison with the Step-Down latency of the group to which the solvent alone was administered and the Step-Down latency of the group to which MK-801 alone was administered.

FIG. 3 shows the learning process of the rats to which Compound 8 that is the agent for improving learning and/or memory according to the present invention, in comparison with the learning process of the rats to which saline was administered.

BEST MODE FOR CARRYING OUT THE INVENTION

Preferred modes of the agent for improving learning and/or memory comprising the isoquinoline derivative of the Formula (I) or a pharmaceutically acceptable acid addition salt thereof, according to the present invention, are as follows:

R¹ is preferably hydrogen, C₁-C₅ alkyl, C₄-C₇ cycloalkylalkyl, C₅-C₇ cycloalkenylalkyl, C₇-C₁₄ aralkyl, C₄-C₅ transalkenyl, allyl, furanyl-2-ylalkyl, thienyl-2-ylalkyl, C₁-C₅ alkanoyl, benzoyl, vinyloxy carbonyl, trichloroethoxycarbonyl, benzyloxy carbonyl or C₈-C₁₄ arylalkanoyl, and especially preferably hydrogen, methyl, ethyl, cyclopropylmethyl, allyl, phenethyl, furan-2-ylethyl or thiophene-2-ylethyl.

R² is preferably hydrogen or OR⁶ (wherein R⁶ represents hydrogen, C₁-C₅ alkyl or C₁-C₅ alkanoyl), especially preferably hydrogen, hydroxy, methoxy or ethoxy.

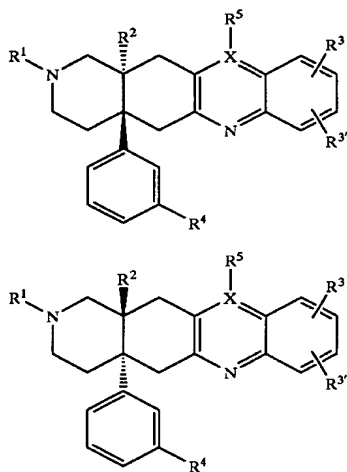
R³ and R^{3'} independently are preferably C₁-C₅ alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxy carbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino, and especially preferably are methyl, hydrogen, chlorine, fluorine, bromine, iodine, hydroxy, methoxy, nitro, amino or dimethylamino.

R⁴ is preferably hydrogen, hydroxy, C₁-C₃ alkoxy, benzyl, C₁-C₅ alkanoyl or halogen, and especially preferably hydrogen, hydroxy or methoxy.

X represents nitrogen or carbon. R⁵ exists only when X is carbon, and is preferably C₁-C₅ alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxy carbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino, and especially preferably methyl, hydrogen, chlorine, fluorine, bromine, iodine, hydroxy, methoxy, nitro, amino or dimethylamino. Needless to say, the compounds of the present invention are not restricted to those mentioned above.

Formula (I) represents relative configuration of the compounds and includes racemic compound and optically active compounds of which absolute structures are represented by the following Formulae (A) and (B). Among these, the optically active compounds represented by the following Formulae (A) are preferred.

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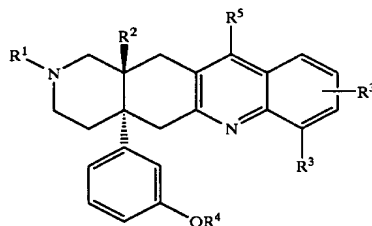
(A)

(B)

Examples of preferred pharmaceutically acceptable acid addition salts include inorganic acid salts such as hydrochloric acid salt, sulfuric acid salt, nitric acid salt, hydrobromic acid salt, hydroiodic acid salt and phosphoric acid salt; organic carboxylic acid salts such as acetic acid salt, lactic acid salt, citric acid salt, oxalic acid salt, glutaric acid salt, malic acid salt, tartaric acid salt, fumaric acid salt, mandelic acid salt, maleic acid salt, benzoic acid salt and phthalic acid salt; and organic sulfonic acid salts such as methanesulfonic acid salt, ethanesulfonic acid salt, benzenesulfonic acid salt, p-toluenesulfonic acid salt and camphorsulfonic acid salt. Among these, hydrochloric acid, hydrobromic acid, phosphoric acid salt, tartaric acid salt, methanesulfonic acid salt and the like are especially preferred, but the pharmaceutically acceptable salts are not restricted to those mentioned above.

The compounds used in the present invention also include the novel compounds represented by Formula (II) below.

(II)



{(A) wherein R¹ represents hydrogen, C₁-C₅ alkyl, C₄-C₇ cycloalkylalkyl, C₅-C₇ cycloalkenylalkyl, C₇-C₁₄ aralkyl, C₄-C₅ transalkenyl, allyl, furanyl-2-ylalkyl, thienyl-2-ylalkyl, C₁-C₅ alkanoyl, benzoyl, vinyloxy carbonyl, trichloroethoxycarbonyl, benzyloxy carbonyl or C₈-C₁₄ arylalkanoyl; R² represents hydrogen or OR⁶ (wherein R⁶ represents hydrogen, C₁-C₅ alkyl or C₁-C₅ alkanoyl); R³ and R^{3'} independently represent C₁-C₅ alkyl, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxy carbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino; R⁴ represents hydrogen or C₁-C₃ alkyl; R⁵ represents C₁-C₅ alkyl, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano,

hydroxy, C₁-C₃ alkoxy, carbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino; or

(B) wherein R¹ represents hydrogen, thienyl-2-ylalkyl, C₁-C₅ alkanoyl, benzoyl, vinylloxycarbonyl, 5 trichloroethoxycarbonyl, benzyloxycarbonyl or C₈-C₁₄ arylalkanoyle; R² represents hydrogen or OR⁶ (wherein R⁶ represents hydrogen, C₁-C₅ alkyl or C₁-C₅ alkanoyl); R³ and R^{3'} independently represent C₁-C₅ alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, 10 hydroxy, C₁-C₃ alkoxy, carbonyl, C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino; R⁴ represents hydrogen or C₁-C₃ alkyl; and R⁵ represents C₁-C₅ alkyl, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C₁-C₃ alkoxy, carbonyl, 15 C₁-C₃ alkylcarbonylamino, C₁-C₅ alkoxy, nitro, amino or C₁-C₃ alkylamino}.

Specific examples of the compounds represented by Formula (II) are shown in Tables 1 to 52.

TABLE 1

Compound No.	R1	R2	R3	R3'	R4	R5
1	Me	H	Cl	5-Cl	H	Me
2	Me	H	Cl	5-Cl	H	NH2
3	Me	H	Cl	5-Cl	H	OH
4	Me	H	Cl	5-Cl	Me	Me
5	Me	H	Cl	5-Cl	Me	NH2
6	Me	H	Cl	5-Cl	Me	OH
7	Me	H	Cl	6-Cl	H	Me
8	Me	H	Cl	6-Cl	H	NH2
9	Me	H	Cl	6-Cl	H	OH
10	Me	H	Cl	6-Cl	Me	Me
11	Me	H	Cl	6-Cl	Me	NH2
12	Me	H	Cl	6-Cl	Me	OH
13	Me	H	Cl	7-Cl	H	Me
14	Me	H	Cl	7-Cl	H	NH2
15	Me	H	Cl	7-Cl	H	OH
16	Me	H	Cl	7-Cl	Me	Me
17	Me	H	Cl	7-Cl	Me	NH2
18	Me	H	Cl	7-Cl	Me	OH
19	Me	H	Cl	5-NH2	H	Me
20	Me	H	Cl	5-NH2	H	NH2
21	Me	H	Cl	5-NH2	H	OH
22	Me	H	Cl	5-NH2	Me	Me
23	Me	H	Cl	5-NH2	Me	NH2
24	Me	H	Cl	5-NH2	Me	OH
25	Me	H	Cl	6-NH2	H	Me
26	Me	H	Cl	6-NH2	H	NH2
27	Me	H	Cl	6-NH2	H	OH
28	Me	H	Cl	6-NH2	Me	Me
29	Me	H	Cl	6-NH2	Me	NH2
30	Me	H	Cl	6-NH2	Me	OH
31	Me	H	Cl	7-NH2	H	Me
32	Me	H	Cl	7-NH2	H	NH2
33	Me	H	Cl	7-NH2	H	OH
34	Me	H	Cl	7-NH2	Me	Me
35	Me	H	Cl	7-NH2	Me	NH2
36	Me	H	Cl	7-NH2	Me	OH
37	Me	H	Cl	5-Me	H	Me
38	Me	H	Cl	5-Me	H	NH2
39	Me	H	Cl	5-Me	H	OH
40	Me	H	Cl	5-Me	Me	Me

TABLE 2

Compound No.	R1	R2	R3	R3'	R4	R5
41	Me	H	Cl	5-Me	Me	NH2
42	Me	H	Cl	5-Me	Me	OH
43	Me	H	Cl	6-Me	H	Me
44	Me	H	Cl	6-Me	H	NH2
45	Me	H	Cl	6-Me	H	OH
46	Me	H	Cl	6-Me	Me	Me

TABLE 2-continued

Compound No.	R1	R2	R3	R3'	R4	R5
47	Me	H	Cl	6-Me	Me	NH2
48	Me	H	Cl	6-Me	Me	OH
49	Me	H	Cl	7-Me	H	Me
50	Me	H	Cl	7-Me	H	NH2
51	Me	H	Cl	7-Me	H	OH
52	Me	H	Cl	7-Me	Me	Me
53	Me	H	Cl	7-Me	Me	NH2
54	Me	H	Cl	7-Me	Me	OH
55	Me	H	NH2	5-Cl	H	Me
56	Me	H	NH2	5-Cl	H	NH2
57	Me	H	NH2	5-Cl	H	OH
58	Me	H	NH2	5-Cl	Me	Me
59	Me	H	NH2	5-Cl	Me	NH2
60	Me	H	NH2	5-Cl	Me	OH
61	Me	H	NH2	6-Cl	H	Me
62	Me	H	NH2	6-Cl	H	NH2
63	Me	H	NH2	6-Cl	H	OH
64	Me	H	NH2	6-Cl	Me	Me
65	Me	H	NH2	6-Cl	Me	NH2
66	Me	H	NH2	6-Cl	Me	OH
67	Me	H	NH2	7-Cl	H	Me
68	Me	H	NH2	7-Cl	H	NH2
69	Me	H	NH2	7-Cl	H	OH
70	Me	H	NH2	7-Cl	Me	Me
71	Me	H	NH2	7-Cl	Me	NH2
72	Me	H	NH2	7-Cl	Me	OH
73	Me	H	NH2	5-NH2	H	Me
74	Me	H	NH2	5-NH2	H	NH2
75	Me	H	NH2	5-NH2	H	OH
76	Me	H	NH2	5-NH2	Me	Me
77	Me	H	NH2	5-NH2	Me	NH2
78	Me	H	NH2	5-NH2	Me	OH
79	Me	H	NH2	6-NH2	H	Me
80	Me	H	NH2	6-NH2	H	NH2

TABLE 3

Compound No.	R1	R2	R3	R3'	R4	R5
81	Me	H	NH2	6-NH2	H	OH
82	Me	H	NH2	6-NH2	Me	Me
83	Me	H	NH2	6-NH2	Me	NH2
84	Me	H	NH2	6-NH2	Me	OH
85	Me	H	NH2	7-NH2	H	Me
86	Me	H	NH2	7-NH2	H	NH2
87	Me	H	NH2	7-NH2	H	OH
88	Me	H	NH2	7-NH2	Me	Me
89	Me	H	NH2	7-NH2	Me	NH2
90	Me	H	NH2	7-NH2	Me	OH
91	Me	H	NH2	5-Me	H	Me
92	Me	H	NH2	5-Me	H	NH2
93	Me	H	NH2	5-Me	H	OH
94	Me	H	NH2	5-Me	Me	Me
95	Me	H	NH2	5-Me	Me	NH2
96	Me	H	NH2	5-Me	Me	OH
97	Me	H	NH2	6-Me	H	Me
98	Me	H	NH2	6-Me	H	NH2
99	Me	H	NH2	6-Me	H	OH
100	Me	H	NH2	6-Me	Me	Me
101	Me	H	NH2	6-Me	Me	NH2
102	Me	H	NH2	6-Me	Me	OH
103	Me	H	NH2	7-Me	H	Me
104	Me	H	NH2	7-Me	H	NH2
105	Me	H	NH2	7-Me	H	OH
106	Me	H	NH2	7-Me	Me	Me
107	Me	H	NH2	7-Me	Me	NH2
108	Me	H	NH2	7-Me	Me	OH
109	Me	H	Me	5-Cl	H	Me
110	Me	H	Me	5-Cl	H	NH2
111	Me	H	Me	5-Cl	H	OH
112	Me	H	Me	5-Cl	Me	Me
113	Me	H	Me	5-Cl	Me	NH2
114	Me	H	Me	5-Cl	Me	OH
115	Me	H	Me	6-Cl	H	Me

TABLE 3-continued

Compound No.	R1	R2	R3	R3'	R4	R5
116	Me	H	Me	6-Cl	H	NH2
117	Me	H	Me	6-Cl	H	OH
118	Me	H	Me	6-Cl	Me	Me
119	Me	H	Me	6-Cl	Me	NH2
120	Me	H	Me	6-Cl	Me	OH

TABLE 4

Compound No.	R1	R2	R3	R3'	R4	R5
121	Me	H	Me	7-Cl	H	Me
122	Me	H	Me	7-Cl	H	NH2
123	Me	H	Me	7-Cl	H	OH
124	Me	H	Me	7-Cl	Me	Me
125	Me	H	Me	7-Cl	Me	NH2
126	Me	H	Me	7-Cl	Me	OH
127	Me	H	Me	5-NH2	H	Me
128	Me	H	Me	5-NH2	H	NH2
129	Me	H	Me	5-NH2	H	OH
130	Me	H	Me	5-NH2	Me	Me
131	Me	H	Me	5-NH2	Me	NH2
132	Me	H	Me	5-NH2	Me	OH
133	Me	H	Me	6-NH2	H	Me
134	Me	H	Me	6-NH2	H	NH2
135	Me	H	Me	6-NH2	H	OH
136	Me	H	Me	6-NH2	Me	Me
137	Me	H	Me	6-NH2	Me	NH2
138	Me	H	Me	6-NH2	Me	OH
139	Me	H	Me	7-NH2	H	Me
140	Me	H	Me	7-NH2	H	NH2
141	Me	H	Me	7-NH2	H	OH
142	Me	H	Me	7-NH2	Me	Me
143	Me	H	Me	7-NH2	Me	NH2
144	Me	H	Me	7-NH2	Me	OH
145	Me	H	Me	5-Me	H	Me
146	Me	H	Me	5-Me	H	NH2
147	Me	H	Me	5-Me	H	OH
148	Me	H	Me	5-Me	Me	Me
149	Me	H	Me	5-Me	Me	NH2
150	Me	H	Me	5-Me	Me	OH
151	Me	H	Me	6-Me	H	Me
152	Me	H	Me	6-Me	H	NH2
153	Me	H	Me	6-Me	H	OH
154	Me	H	Me	6-Me	Me	Me
155	Me	H	Me	6-Me	Me	NH2
156	Me	H	Me	6-Me	Me	OH
157	Me	H	Me	7-Me	H	Me
158	Me	H	Me	7-Me	H	NH2
159	Me	H	Me	7-Me	H	OH
160	Me	H	Me	7-Me	Me	Me

TABLE 5

Compound No.	R1	R2	R3	R3'	R4	R5
161	Me	H	Me	7-Me	Me	NH2
162	Me	H	Me	7-Me	Me	OH
163	Me	OH	Cl	5-Cl	H	Me
164	Me	OH	Cl	5-Cl	H	NH2
165	Me	OH	Cl	5-Cl	H	OH
166	Me	OH	Cl	5-Cl	Me	Me
167	Me	OH	Cl	5-Cl	Me	NH2
168	Me	OH	Cl	5-Cl	Me	OH
169	Me	OH	Cl	6-Cl	H	Me
170	Me	OH	Cl	6-Cl	H	NH2
171	Me	OH	Cl	6-Cl	H	OH
172	Me	OH	Cl	6-Cl	Me	Me
173	Me	OH	Cl	6-Cl	Me	NH2
174	Me	OH	Cl	6-Cl	Me	OH
175	Me	OH	Cl	7-Cl	H	Me
176	Me	OH	Cl	7-Cl	H	NH2
177	Me	OH	Cl	7-Cl	H	OH

TABLE 5-continued

Compound No.	R1	R2	R3	R3'	R4	R5
178	Me	OH	Cl	7-Cl	Me	Me
179	Me	OH	Cl	7-Cl	Me	NH2
180	Me	OH	Cl	7-Cl	Me	OH
181	Me	OH	Cl	5-NH2	H	Me
182	Me	OH	Cl	5-NH2	H	NH2
183	Me	OH	Cl	5-NH2	H	OH
184	Me	OH	Cl	5-NH2	Me	Me
185	Me	OH	Cl	5-NH2	Me	NH2
186	Me	OH	Cl	5-NH2	Me	OH
187	Me	OH	Cl	6-NH2	H	Me
188	Me	OH	Cl	6-NH2	H	NH2
189	Me	OH	Cl	6-NH2	H	OH
190	Me	OH	Cl	6-NH2	Me	Me
191	Me	OH	Cl	6-NH2	Me	NH2
192	Me	OH	Cl	6-NH2	Me	OH
193	Me	OH	Cl	7-NH2	H	Me
194	Me	OH	Cl	7-NH2	H	NH2
195	Me	OH	Cl	7-NH2	H	OH
196	Me	OH	Cl	7-NH2	Me	Me
197	Me	OH	Cl	7-NH2	Me	NH2
198	Me	OH	Cl	7-NH2	Me	OH
199	Me	OH	Cl	5-Me	H	Me
200	Me	OH	Cl	5-Me	H	NH2

TABLE 6

Compound No.	R1	R2	R3	R3'	R4	R5
201	Me	OH	Cl	5-Me	H	OH
202	Me	OH	Cl	5-Me	Me	Me
203	Me	OH	Cl	5-Me	Me	NH2
204	Me	OH	Cl	5-Me	Me	OH
205	Me	OH	Cl	6-Me	H	Me
206	Me	OH	Cl	6-Me	H	NH2
207	Me	OH	Cl	6-Me	H	OH
208	Me	OH	Cl	6-Me	Me	Me
209	Me	OH	Cl	6-Me	Me	NH2
210	Me	OH	Cl	6-Me	Me	OH
211	Me	OH	Cl	7-Me	H	Me
212	Me	OH	Cl	7-Me	H	NH2
213	Me	OH	Cl	7-Me	H	OH
214	Me	OH	Cl	7-Me	Me	Me
215	Me	OH	Cl	7-Me	Me	NH2
216	Me	OH	Cl	7-Me	Me	OH
217	Me	OH	NH2	5-Cl	H	Me
218	Me	OH	NH2	5-Cl	H	NH2
219	Me	OH	NH2	5-Cl	H	OH
220	Me	OH	NH2	5-Cl	Me	Me
221	Me	OH	NH2	5-Cl	Me	NH2
222	Me	OH	NH2	5-Cl	Me	OH
223	Me	OH	NH2	6-Cl	H	Me
224	Me	OH	NH2	6-Cl	H	NH2
225	Me	OH	NH2	6-Cl	H	OH
226	Me	OH	NH2	6-Cl	Me	Me
227	Me	OH	NH2	6-Cl	Me	NH2
228	Me	OH	NH2	6-Cl	Me	OH
229	Me	OH	NH2	7-Cl	H	Me
230	Me	OH	NH2	7-Cl	H	NH2
231	Me	OH	NH2	7-Cl	H	OH
232	Me	OH	NH2	7-Cl	Me	Me
233	Me	OH	NH2	7-Cl	Me	NH2
234	Me	OH	NH2	7-Cl	Me	OH
235	Me	OH	NH2	5-NH2	H	Me
236	Me	OH	NH2	5-NH2	H	NH2
237	Me	OH	NH2	5-NH2	H	OH
238	Me	OH	NH2	5-NH2	Me	Me
239	Me	OH	NH2	5-NH2	Me	NH2
240	Me	OH	NH2	5-NH2	Me	OH

TABLE 7

Compound No.	R1	R2	R3	R3'	R4	R5
241	Me	OH	NH2	6-NH2	H	Me
242	Me	OH	NH2	6-NH2	H	NH2
243	Me	OH	NH2	6-NH2	H	OH
244	Me	OH	NH2	6-NH2	Me	Me
245	Me	OH	NH2	6-NH2	Me	NH2
246	Me	OH	NH2	6-NH2	Me	OH
247	Me	OH	NH2	7-NH2	H	Me
248	Me	OH	NH2	7-NH2	H	NH2
249	Me	OH	NH2	7-NH2	H	OH
250	Me	OH	NH2	7-NH2	Me	Me
251	Me	OH	NH2	7-NH2	Me	NH2
252	Me	OH	NH2	7-NH2	Me	OH
253	Me	OH	NH2	5-Me	H	Me
254	Me	OH	NH2	5-Me	H	NH2
255	Me	OH	NH2	5-Me	H	OH
256	Me	OH	NH2	5-Me	Me	Me
257	Me	OH	NH2	5-Me	Me	NH2
258	Me	OH	NH2	5-Me	Me	OH
259	Me	OH	NH2	6-Me	H	Me
260	Me	OH	NH2	6-Me	H	NH2
261	Me	OH	NH2	6-Me	H	OH
262	Me	OH	NH2	6-Me	Me	Me
263	Me	OH	NH2	6-Me	Me	NH2
264	Me	OH	NH2	6-Me	Me	OH
265	Me	OH	NH2	7-Me	H	Me
266	Me	OH	NH2	7-Me	H	NH2
267	Me	OH	NH2	7-Me	H	OH
268	Me	OH	NH2	7-Me	Me	Me
269	Me	OH	NH2	7-Me	Me	NH2
270	Me	OH	NH2	7-Me	Me	OH
271	Me	OH	Me	5-Cl	H	Me
272	Me	OH	Me	5-Cl	H	NH2
273	Me	OH	Me	5-Cl	H	OH
274	Me	OH	Me	5-Cl	Me	Me
275	Me	OH	Me	5-Cl	Me	NH2
276	Me	OH	Me	5-Cl	Me	OH
277	Me	OH	Me	6-Cl	H	Me
278	Me	OH	Me	6-Cl	H	NH2
279	Me	OH	Me	6-Cl	H	OH
280	Me	OH	Me	6-Cl	Me	Me

TABLE 8

Compound No.	R1	R2	R3	R3'	R4	R5
281	Me	OH	Me	6-Cl	Me	NH2
282	Me	OH	Me	6-Cl	Me	OH
283	Me	OH	Me	7-Cl	H	Me
284	Me	OH	Me	7-Cl	H	NH2
285	Me	OH	Me	7-Cl	H	OH
286	Me	OH	Me	7-Cl	Me	Me
287	Me	OH	Me	7-Cl	Me	NH2
288	Me	OH	Me	7-Cl	Me	OH
289	Me	OH	Me	5-NH2	H	Me
290	Me	OH	Me	5-NH2	H	NH2
291	Me	OH	Me	5-NH2	H	OH
292	Me	OH	Me	5-NH2	Me	Me
293	Me	OH	Me	5-NH2	Me	NH2
294	Me	OH	Me	5-NH2	Me	OH
295	Me	OH	Me	6-NH2	H	Me
296	Me	OH	Me	6-NH2	H	NH2
297	Me	OH	Me	6-NH2	H	OH
298	Me	OH	Me	6-NH2	Me	Me
299	Me	OH	Me	6-NH2	Me	NH2
300	Me	OH	Me	6-NH2	Me	OH
301	Me	OH	Me	7-NH2	H	Me
302	Me	OH	Me	7-NH2	H	NH2
303	Me	OH	Me	7-NH2	H	OH
304	Me	OH	Me	7-NH2	Me	Me
305	Me	OH	Me	7-NH2	Me	NH2
306	Me	OH	Me	7-NH2	Me	OH
307	Me	OH	Me	5-Me	H	Me
308	Me	OH	Me	5-Me	H	NH2
309	Me	OH	Me	5-Me	H	OH

TABLE 8-continued

Compound No.	R1	R2	R3	R3'	R4	R5
310	Me	OH	Me	5-Me	Me	Me
311	Me	OH	Me	5-Me	Me	NH2
312	Me	OH	Me	5-Me	Me	OH
313	Me	OH	Me	6-Me	H	Me
314	Me	OH	Me	6-Me	H	NH2
315	Me	OH	Me	6-Me	H	OH
316	Me	OH	Me	6-Me	Me	Me
317	Me	OH	Me	6-Me	Me	NH2
318	Me	OH	Me	6-Me	Me	OH
319	Me	OH	Me	7-Me	H	Me
320	Me	OH	Me	7-Me	H	NH2

TABLE 9

Compound No.	R1	R2	R3	R3'	R4	R5
321	Me	OH	Me	7-Me	H	OH
322	Me	OH	Me	7-Me	Me	Me
323	Me	OH	Me	7-Me	Me	NH2
324	Me	OH	Me	7-Me	Me	OH
325	Me	OMe	Cl	5-Cl	H	Me
326	Me	OMe	Cl	5-Cl	H	NH2
327	Me	OMe	Cl	5-Cl	H	OH
328	Me	OMe	Cl	5-Cl	Me	Me
329	Me	OMe	Cl	5-Cl	Me	NH2
330	Me	OMe	Cl	5-Cl	Me	OH
331	Me	OMe	Cl	6-Cl	H	Me
332	Me	OMe	Cl	6-Cl	H	NH2
333	Me	OMe	Cl	6-Cl	H	OH
334	Me	OMe	Cl	6-Cl	Me	Me
335	Me	OMe	Cl	6-Cl	Me	NH2
336	Me	OMe	Cl	6-Cl	Me	OH
337	Me	OMe	Cl	7-Cl	H	Me
338	Me	OMe	Cl	7-Cl	H	NH2
339	Me	OMe	Cl	7-Cl	H	OH
340	Me	OMe	Cl	7-Cl	Me	Me
341	Me	OMe	Cl	7-Cl	Me	NH2
342	Me	OMe	Cl	7-Cl	Me	OH
343	Me	OMe	Cl	5-NH2	H	Me
344	Me	OMe	Cl	5-NH2	H	NH2
345	Me	OMe	Cl	5-NH2	H	OH
346	Me	OMe	Cl	5-NH2	Me	Me
347	Me	OMe	Cl	5-NH2	Me	NH2
348	Me	OMe	Cl	5-NH2	Me	OH
349	Me	OMe	Cl	6-NH2	H	Me
350	Me	OMe	Cl	6-NH2	H	NH2
351	Me	OMe	Cl	6-NH2	H	OH
352	Me	OMe	Cl	6-NH2	Me	Me
353	Me	OMe	Cl	6-NH2	Me	NH2
354	Me	OMe	Cl	6-NH2	Me	OH
355	Me	OMe	Cl	7-NH2	H	Me
356	Me	OMe	Cl	7-NH2	H	NH2
357	Me	OMe	Cl	7-NH2	H	OH
358	Me	OMe	Cl	7-NH2	Me	Me
359	Me	OMe	Cl	7-NH2	Me	NH2
360	Me	OMe	Cl	7-NH2	Me	OH

TABLE 10

Compound No.	R1	R2	R3	R3'	R4	R5
361	Me	OMe	Cl	5-Me	H	Me
362	Me	OMe	Cl	5-Me	H	NH2
363	Me	OMe	Cl	5-Me	H	OH
364	Me	OMe	Cl	5-Me	Me	Me
365	Me	OMe	Cl	5-Me	Me	NH2
366	Me	OMe	Cl	5-Me	Me	OH
367	Me	OMe	Cl	6-Me	H	Me
368	Me	OMe	Cl	6-Me	H	NH2
369	Me	OMe	Cl	6-Me	H	OH
370	Me	OMe	Cl	6-Me	Me	Me
371	Me	OMe	Cl	6-Me	Me	NH2

11

TABLE 10-continued

Compound No.	R1	R2	R3	R3'	R4	R5
372	Me	OMe	Cl	6-Me	Me	OH
373	Me	OMe	Cl	7-Me	H	Me
374	Me	OMe	Cl	7-Me	H	NH2
375	Me	OMe	Cl	7-Me	H	OH
376	Me	OMe	Cl	7-Me	Me	Me
377	Me	OMe	Cl	7-Me	Me	NH2
378	Me	OMe	Cl	7-Me	Me	OH
379	Me	OMe	NH2	5-Cl	H	Me
380	Me	OMe	NH2	5-Cl	H	NH2
381	Me	OMe	NH2	5-Cl	H	OH
382	Me	OMe	NH2	5-Cl	Me	Me
383	Me	OMe	NH2	5-Cl	Me	NH2
384	Me	OMe	NH2	5-Cl	Me	OH
385	Me	OMe	NH2	6-Cl	H	Me
386	Me	OMe	NH2	6-Cl	H	NH2
387	Me	OMe	NH2	6-Cl	H	OH
388	Me	OMe	NH2	6-Cl	Me	Me
389	Me	OMe	NH2	6-Cl	Me	NH2
390	Me	OMe	NH2	6-Cl	Me	OH
391	Me	OMe	NH2	7-Cl	H	Me
392	Me	OMe	NH2	7-Cl	H	NH2
393	Me	OMe	NH2	7-Cl	H	OH
394	Me	OMe	NH2	7-Cl	Me	Me
395	Me	OMe	NH2	7-Cl	Me	NH2
396	Me	OMe	NH2	7-Cl	Me	OH
397	Me	OMe	NH2	5-NH2	H	Me
398	Me	OMe	NH2	5-NH2	H	NH2
399	Me	OMe	NH2	5-NH2	H	OH
400	Me	OMe	NH2	5-NH2	Me	Me

TABLE 11

Compound No.	R1	R2	R3	R3'	R4	R5
401	Me	OMe	NH2	5-NH2	Me	NH2
402	Me	OMe	NH2	5-NH2	Me	OH
403	Me	OMe	NH2	6-NH2	H	Me
404	Me	OMe	NH2	6-NH2	H	NH2
405	Me	OMe	NH2	6-NH2	H	OH
406	Me	OMe	NH2	6-NH2	Me	Me
407	Me	OMe	NH2	6-NH2	Me	NH2
408	Me	OMe	NH2	6-NH2	Me	OH
409	Me	OMe	NH2	7-NH2	H	Me
410	Me	OMe	NH2	7-NH2	H	NH2
411	Me	OMe	NH2	7-NH2	H	OH
412	Me	OMe	NH2	7-NH2	Me	Me
413	Me	OMe	NH2	7-NH2	Me	NH2
414	Me	OMe	NH2	7-NH2	Me	OH
415	Me	OMe	NH2	5-Me	H	Me
416	Me	OMe	NH2	5-Me	H	NH2
417	Me	OMe	NH2	5-Me	H	OH
418	Me	OMe	NH2	5-Me	Me	Me
419	Me	OMe	NH2	5-Me	Me	NH2
420	Me	OMe	NH2	5-Me	Me	OH
421	Me	OMe	NH2	6-Me	H	Me
422	Me	OMe	NH2	6-Me	H	NH2
423	Me	OMe	NH2	6-Me	H	OH
424	Me	OMe	NH2	6-Me	Me	Me
425	Me	OMe	NH2	6-Me	Me	NH2
426	Me	OMe	NH2	6-Me	Me	OH
427	Me	OMe	NH2	7-Me	H	Me
428	Me	OMe	NH2	7-Me	H	NH2
429	Me	OMe	NH2	7-Me	H	OH
430	Me	OMe	NH2	7-Me	Me	Me
431	Me	OMe	NH2	7-Me	Me	NH2
432	Me	OMe	NH2	7-Me	Me	OH
433	Me	OMe	Me	5-Cl	H	Me
434	Me	OMe	Me	5-Cl	H	NH2
435	Me	OMe	Me	5-Cl	H	OH
436	Me	OMe	Me	5-Cl	Me	Me
437	Me	OMe	Me	5-Cl	Me	NH2
438	Me	OMe	Me	5-Cl	Me	OH

12

TABLE 11-continued

Compound No.	R1	R2	R3	R3'	R4	R5
439	Me	OMe	Me	6-Cl	H	Me
440	Me	OMe	Me	6-Cl	H	NH2

TABLE 12

Compound No.	R1	R2	R3	R3'	R4	R5
441	Me	OMe	Me	6-Cl	H	OH
442	Me	OMe	Me	6-Cl	Me	Me
443	Me	OMe	Me	6-Cl	Me	NH2
444	Me	OMe	Me	6-Cl	Me	OH
445	Me	OMe	Me	7-Cl	H	Me
446	Me	OMe	Me	7-Cl	H	NH2
447	Me	OMe	Me	7-Cl	H	OH
448	Me	OMe	Me	7-Cl	Me	Me
449	Me	OMe	Me	7-Cl	Me	NH2
450	Me	OMe	Me	7-Cl	Me	OH
451	Me	OMe	Me	5-NH2	H	Me
452	Me	OMe	Me	5-NH2	H	NH2
453	Me	OMe	Me	5-NH2	H	OH
454	Me	OMe	Me	5-NH2	Me	Me
455	Me	OMe	Me	5-NH2	Me	NH2
456	Me	OMe	Me	5-NH2	Me	OH
457	Me	OMe	Me	6-NH2	H	Me
458	Me	OMe	Me	6-NH2	H	NH2
459	Me	OMe	Me	6-NH2	H	OH
460	Me	OMe	Me	6-NH2	Me	Me
461	Me	OMe	Me	6-NH2	Me	NH2
462	Me	OMe	Me	6-NH2	Me	OH
463	Me	OMe	Me	7-NH2	H	Me
464	Me	OMe	Me	7-NH2	H	NH2
465	Me	OMe	Me	7-NH2	H	OH
466	Me	OMe	Me	7-NH2	Me	Me
467	Me	OMe	Me	7-NH2	Me	NH2
468	Me	OMe	Me	7-NH2	Me	OH
469	Me	OMe	Me	5-Me	H	Me
470	Me	OMe	Me	5-Me	H	NH2
471	Me	OMe	Me	5-Me	H	OH
472	Me	OMe	Me	5-Me	Me	Me
473	Me	OMe	Me	5-Me	Me	NH2
474	Me	OMe	Me	5-Me	Me	OH
475	Me	OMe	Me	6-Me	H	Me
476	Me	OMe	Me	6-Me	H	NH2
477	Me	OMe	Me	6-Me	H	OH
478	Me	OMe	Me	6-Me	Me	Me
479	Me	OMe	Me	6-Me	Me	NH2
480	Me	OMe	Me	6-Me	Me	OH

TABLE 13

Compound No.	R1	R2	R3	R3'	R4	R5
481	Me	OMe	Me	7-Me	H	Me
482	Me	OMe	Me	7-Me	H	NH2
483	Me	OMe	Me	7-Me	H	OH
484	Me	OMe	Me	7-Me	Me	Me
485	Me	OMe	Me	7-Me	Me	NH2
486	Me	OMe	Me	7-Me	Me	OH
487	CH2CH2Ph	H	Cl	5-Cl	H	Me
488	CH2CH2Ph	H	Cl	5-Cl	H	NH2
489	CH2CH2Ph	H	Cl	5-Cl	H	OH
490	CH2CH2Ph	H	Cl	5-Cl	Me	Me
491	CH2CH2Ph	H	Cl	5-Cl	Me	NH2
492	CH2CH2Ph	H	Cl	5-Cl	Me	OH
493	CH2CH2Ph	H	Cl	6-Cl	H	Me
494	CH2CH2Ph	H	Cl	6-Cl	H	NH2
495	CH2CH2Ph	H	Cl	6-Cl	H	OH
496	CH2CH2Ph	H	Cl	6-Cl	Me	Me
497	CH2CH2Ph	H	Cl	6-Cl	Me	NH2
498	CH2CH2Ph	H	Cl	6-Cl	Me	OH
499	CH2CH2Ph	H	Cl	7-Cl	H	Me
500	CH2CH2Ph	H	Cl	7-Cl	H	NH2

TABLE 13-continued

Compound No.	R1	R2	R3	R3'	R4	R5
501	CH ₂ CH ₂ Ph	H	Cl	7-Cl	H	OH
502	CH ₂ CH ₂ Ph	H	Cl	7-Cl	Me	Me
503	CH ₂ CH ₂ Ph	H	Cl	7-Cl	Me	NH ₂
504	CH ₂ CH ₂ Ph	H	Cl	7-Cl	Me	OH
505	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	H	Me
506	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	H	NH ₂
507	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	H	OH
508	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	Me	Me
509	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	Me	NH ₂
510	CH ₂ CH ₂ Ph	H	Cl	5-NH ₂	Me	OH
511	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	H	Me
512	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	H	NH ₂
513	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	H	OH
514	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	Me	Me
515	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	Me	NH ₂
516	CH ₂ CH ₂ Ph	H	Cl	6-NH ₂	Me	OH
517	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	H	Me
518	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	H	NH ₂
519	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	H	OH
520	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	Me	Me

TABLE 14

Compound No.	R1	R2	R3	R3'	R4	R5
521	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	Me	NH ₂
522	CH ₂ CH ₂ Ph	H	Cl	7-NH ₂	Me	OH
523	CH ₂ CH ₂ Ph	H	Cl	5-Me	H	Me
524	CH ₂ CH ₂ Ph	H	Cl	5-Me	H	NH ₂
525	CH ₂ CH ₂ Ph	H	Cl	5-Me	H	OH
526	CH ₂ CH ₂ Ph	H	Cl	5-Me	Me	Me
527	CH ₂ CH ₂ Ph	H	Cl	5-Me	Me	NH ₂
528	CH ₂ CH ₂ Ph	H	Cl	5-Me	Me	OH
529	CH ₂ CH ₂ Ph	H	Cl	6-Me	H	Me
530	CH ₂ CH ₂ Ph	H	Cl	6-Me	H	NH ₂
531	CH ₂ CH ₂ Ph	H	Cl	6-Me	H	OH
532	CH ₂ CH ₂ Ph	H	Cl	6-Me	Me	Me
533	CH ₂ CH ₂ Ph	H	Cl	6-Me	Me	NH ₂
534	CH ₂ CH ₂ Ph	H	Cl	6-Me	Me	OH
535	CH ₂ CH ₂ Ph	H	Cl	7-Me	H	Me
536	CH ₂ CH ₂ Ph	H	Cl	7-Me	H	NH ₂
537	CH ₂ CH ₂ Ph	H	Cl	7-Me	H	OH
538	CH ₂ CH ₂ Ph	H	Cl	7-Me	Me	Me
539	CH ₂ CH ₂ Ph	H	Cl	7-Me	Me	NH ₂
540	CH ₂ CH ₂ Ph	H	Cl	7-Me	Me	OH
541	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	H	Me
542	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	H	NH ₂
543	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	H	OH
544	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	Me	Me
545	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	Me	NH ₂
546	CH ₂ CH ₂ Ph	H	NH ₂	5-Cl	Me	OH
547	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	H	Me
548	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	H	NH ₂
549	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	H	OH
550	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	Me	Me
551	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	Me	NH ₂
552	CH ₂ CH ₂ Ph	H	NH ₂	6-Cl	Me	OH
553	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	H	Me
554	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	H	NH ₂
555	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	H	OH
556	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	Me	Me
557	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	Me	NH ₂
558	CH ₂ CH ₂ Ph	H	NH ₂	7-Cl	Me	OH
559	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	H	Me
560	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	H	NH ₂

TABLE 15

Compound No.	R1	R2	R3	R3'	R4	R5
561	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	H	OH
562	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	Me	Me

TABLE 15-continued

Compound No.	R1	R2	R3	R3'	R4	R5
563	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	Me	NH ₂
564	CH ₂ CH ₂ Ph	H	NH ₂	5-NH ₂	Me	OH
565	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	H	Me
566	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	H	NH ₂
567	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	H	OH
568	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	Me	Me
569	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	Me	NH ₂
570	CH ₂ CH ₂ Ph	H	NH ₂	6-NH ₂	Me	OH
571	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	H	Me
572	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	H	NH ₂
573	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	H	OH
574	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	Me	Me
575	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	Me	NH ₂
576	CH ₂ CH ₂ Ph	H	NH ₂	7-NH ₂	Me	OH
577	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	H	Me
578	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	H	NH ₂
579	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	H	OH
580	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	Me	Me
581	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	Me	NH ₂
582	CH ₂ CH ₂ Ph	H	NH ₂	5-Me	Me	OH
583	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	H	Me
584	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	H	NH ₂
585	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	H	OH
586	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	Me	Me
587	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	Me	NH ₂
588	CH ₂ CH ₂ Ph	H	NH ₂	6-Me	Me	OH
589	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	H	Me
590	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	H	NH ₂
591	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	H	OH
592	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	Me	Me
593	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	Me	NH ₂
594	CH ₂ CH ₂ Ph	H	NH ₂	7-Me	Me	OH
595	CH ₂ CH ₂ Ph	H	Me	5-Cl	H	Me
596	CH ₂ CH ₂ Ph	H	Me	5-Cl	H	NH ₂
597	CH ₂ CH ₂ Ph	H	Me	5-Cl	H	OH
598	CH ₂ CH ₂ Ph	H	Me	5-Cl	Me	Me
599	CH ₂ CH ₂ Ph	H	Me	5-Cl	Me	NH ₂
600	CH ₂ CH ₂ Ph	H	Me	5-Cl	Me	OH

TABLE 16

Compound No.	R1	R2	R3	R3'	R4	R5
601	CH ₂ CH ₂ Ph	H	Me	6-Cl	H	Me
602	CH ₂ CH ₂ Ph	H	Me	6-Cl	H	NH ₂
603	CH ₂ CH ₂ Ph	H	Me	6-Cl	H	OH
604	CH ₂ CH ₂ Ph	H	Me	6-Cl	Me	Me
605	CH ₂ CH ₂ Ph	H	Me	6-Cl	Me	NH ₂
606	CH ₂ CH ₂ Ph	H	Me	6-Cl	Me	OH
607	CH ₂ CH ₂ Ph	H	Me	7-Cl	H	Me
608	CH ₂ CH ₂ Ph	H	Me	7-Cl	H	NH ₂
609	CH ₂ CH ₂ Ph	H	Me	7-Cl	H	OH
610	CH ₂ CH ₂ Ph	H	Me	7-Cl	Me	Me
611	CH ₂ CH ₂ Ph	H	Me	7-Cl	Me	NH ₂
612	CH ₂ CH ₂ Ph	H	Me	7-Cl	Me	OH
613	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	H	Me
614	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	H	NH ₂
615	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	H	OH
616	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	Me	Me
617	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	Me	NH ₂
618	CH ₂ CH ₂ Ph	H	Me	5-NH ₂	Me	OH
619	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	H	Me
620	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	H	NH ₂
621	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	H	OH
622	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	Me	Me
623	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	Me	NH ₂
624	CH ₂ CH ₂ Ph	H	Me	6-NH ₂	Me	OH
625	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	H	Me
626	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	H	NH ₂
627	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	H	OH
628	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	Me	Me
629	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	Me	NH ₂
630	CH ₂ CH ₂ Ph	H	Me	7-NH ₂	Me	OH
631	CH ₂ CH ₂ Ph	H	Me	5-Me	H	Me

TABLE 16-continued

Compound No.	R1	R2	R3	R3'	R4	R5
632	CH ₂ CH ₂ Ph	H	Me	5-Me	H	NH ₂
633	CH ₂ CH ₂ Ph	H	Me	5-Me	H	OH
634	CH ₂ CH ₂ Ph	H	Me	5-Me	Me	Me
635	CH ₂ CH ₂ Ph	H	Me	5-Me	Me	NH ₂
636	CH ₂ CH ₂ Ph	H	Me	5-Me	Me	OH
637	CH ₂ CH ₂ Ph	H	Me	6-Me	H	Me
638	CH ₂ CH ₂ Ph	H	Me	6-Me	H	NH ₂
639	CH ₂ CH ₂ Ph	H	Me	6-Me	H	OH
640	CH ₂ CH ₂ Ph	H	Me	6-Me	Me	Me

TABLE 17

Compound No.	R1	R2	R3	R3'	R4	R5
641	CH ₂ CH ₂ Ph	H	Me	6-Me	Me	NH ₂
642	CH ₂ CH ₂ Ph	H	Me	6-Me	Me	OH
643	CH ₂ CH ₂ Ph	H	Me	7-Me	H	Me
644	CH ₂ CH ₂ Ph	H	Me	7-Me	H	NH ₂
645	CH ₂ CH ₂ Ph	H	Me	7-Me	H	OH
646	CH ₂ CH ₂ Ph	H	Me	7-Me	Me	Me
647	CH ₂ CH ₂ Ph	H	Me	7-Me	Me	NH ₂
648	CH ₂ CH ₂ Ph	H	Me	7-Me	Me	OH
649	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	H	Me
650	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	H	NH ₂
651	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	H	OH
652	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	Me	Me
653	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	Me	NH ₂
654	CH ₂ CH ₂ Ph	OH	Cl	5-Cl	Me	OH
655	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	H	Me
656	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	H	NH ₂
657	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	H	OH
658	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	Me	Me
659	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	Me	NH ₂
660	CH ₂ CH ₂ Ph	OH	Cl	6-Cl	Me	OH
661	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	H	Me
662	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	H	NH ₂
663	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	H	OH
664	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	Me	Me
665	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	Me	NH ₂
666	CH ₂ CH ₂ Ph	OH	Cl	7-Cl	Me	OH
667	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	H	Me
668	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	H	NH ₂
669	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	H	OH
670	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	Me	Me
671	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	Me	NH ₂
672	CH ₂ CH ₂ Ph	OH	Cl	5-NH ₂	Me	OH
673	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	H	Me
674	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	H	NH ₂
675	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	H	OH
676	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	Me	Me
677	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	Me	NH ₂
678	CH ₂ CH ₂ Ph	OH	Cl	6-NH ₂	Me	OH
679	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	H	Me
680	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	H	NH ₂

TABLE 18

Compound No.	R1	R2	R3	R3'	R4	R5
681	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	H	OH
682	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	Me	Me
683	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	Me	NH ₂
684	CH ₂ CH ₂ Ph	OH	Cl	7-NH ₂	Me	OH
685	CH ₂ CH ₂ Ph	OH	Cl	5-Me	H	Me
686	CH ₂ CH ₂ Ph	OH	Cl	5-Me	H	NH ₂
687	CH ₂ CH ₂ Ph	OH	Cl	5-Me	H	OH
688	CH ₂ CH ₂ Ph	OH	Cl	5-Me	Me	Me
689	CH ₂ CH ₂ Ph	OH	Cl	5-Me	Me	NH ₂
690	CH ₂ CH ₂ Ph	OH	Cl	5-Me	Me	OH
691	CH ₂ CH ₂ Ph	OH	Cl	6-Me	H	Me
692	CH ₂ CH ₂ Ph	OH	Cl	6-Me	H	NH ₂
693	CH ₂ CH ₂ Ph	OH	Cl	6-Me	H	OH

TABLE 18-continued

Compound No.	R1	R2	R3	R3'	R4	R5
694	CH ₂ CH ₂ Ph	OH	Cl	6-Me	Me	Me
695	CH ₂ CH ₂ Ph	OH	Cl	6-Me	Me	NH ₂
696	CH ₂ CH ₂ Ph	OH	Cl	6-Me	Me	OH
697	CH ₂ CH ₂ Ph	OH	Cl	7-Me	H	Me
698	CH ₂ CH ₂ Ph	OH	Cl	7-Me	H	NH ₂
699	CH ₂ CH ₂ Ph	OH	Cl	7-Me	H	OH
700	CH ₂ CH ₂ Ph	OH	Cl	7-Me	Me	Me
701	CH ₂ CH ₂ Ph	OH	Cl	7-Me	Me	NH ₂
702	CH ₂ CH ₂ Ph	OH	Cl	7-Me	Me	OH
703	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	H	Me
704	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	H	NH ₂
705	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	H	OH
706	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	Me	Me
707	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	Me	NH ₂
708	CH ₂ CH ₂ Ph	OH	NH ₂	5-Cl	Me	OH
709	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	H	Me
710	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	H	NH ₂
711	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	H	OH
712	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	Me	Me
713	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	Me	NH ₂
714	CH ₂ CH ₂ Ph	OH	NH ₂	6-Cl	Me	OH
715	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	H	Me
716	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	H	NH ₂
717	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	H	OH
718	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	Me	Me
719	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	Me	NH ₂
720	CH ₂ CH ₂ Ph	OH	NH ₂	7-Cl	Me	OH

TABLE 19

Compound No.	R1	R2	R3	R3'	R4	R5
721	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	H	Me
722	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	H	NH ₂
723	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	H	OH
724	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	Me	Me
725	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	Me	NH ₂
726	CH ₂ CH ₂ Ph	OH	NH ₂	5-NH ₂	Me	OH
727	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	H	Me
728	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	H	NH ₂
729	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	H	OH
730	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	Me	Me
731	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	Me	NH ₂
732	CH ₂ CH ₂ Ph	OH	NH ₂	6-NH ₂	Me	OH
733	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	H	Me
734	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	H	NH ₂
735	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	H	OH
736	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	Me	Me
737	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	Me	NH ₂
738	CH ₂ CH ₂ Ph	OH	NH ₂	7-NH ₂	Me	OH
739	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	H	Me
740	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	H	NH ₂
741	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	H	OH
742	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	Me	Me
743	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	Me	NH ₂
744	CH ₂ CH ₂ Ph	OH	NH ₂	5-Me	Me	OH
745	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	H	Me
746	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	H	NH ₂
747	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	H	OH
748	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	Me	Me
749	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	Me	NH ₂
750	CH ₂ CH ₂ Ph	OH	NH ₂	6-Me	Me	OH
751	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	H	Me
752	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	H	NH ₂
753	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	H	OH
754	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	Me	Me
755	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	Me	NH ₂
756	CH ₂ CH ₂ Ph	OH	NH ₂	7-Me	Me	OH
757	CH ₂ CH ₂ Ph	OH	Me	5-Cl	H	Me
758	CH ₂ CH ₂ Ph	OH	Me	5-Cl	H	NH ₂
759	CH ₂ CH ₂ Ph	OH	Me	5-Cl	H	OH
760	CH ₂ CH ₂ Ph	OH	Me	5-Cl	Me	Me

TABLE 20

Compound No.	R1	R2	R3	R3'	R4	R5
761	CH ₂ CH ₂ Ph	OH	Me	5-Cl	Me	NH ₂
762	CH ₂ CH ₂ Ph	OH	Me	5-Cl	Me	OH
763	CH ₂ CH ₂ Ph	OH	Me	6-Cl	H	Me
764	CH ₂ CH ₂ Ph	OH	Me	6-Cl	H	NH ₂
765	CH ₂ CH ₂ Ph	OH	Me	6-Cl	H	OH
766	CH ₂ CH ₂ Ph	OH	Me	6-Cl	Me	Me
767	CH ₂ CH ₂ Ph	OH	Me	6-Cl	Me	NH ₂
768	CH ₂ CH ₂ Ph	OH	Me	6-Cl	Me	OH
769	CH ₂ CH ₂ Ph	OH	Me	7-Cl	H	Me
770	CH ₂ CH ₂ Ph	OH	Me	7-Cl	H	NH ₂
771	CH ₂ CH ₂ Ph	OH	Me	7-Cl	H	OH
772	CH ₂ CH ₂ Ph	OH	Me	7-Cl	Me	Me
773	CH ₂ CH ₂ Ph	OH	Me	7-Cl	Me	NH ₂
774	CH ₂ CH ₂ Ph	OH	Me	7-Cl	Me	OH
775	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	H	Me
776	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	H	NH ₂
777	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	H	OH
778	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	Me	Me
779	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	Me	NH ₂
780	CH ₂ CH ₂ Ph	OH	Me	5-NH ₂	Me	OH
781	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	H	Me
782	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	H	NH ₂
783	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	H	OH
784	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	Me	Me
785	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	Me	NH ₂
786	CH ₂ CH ₂ Ph	OH	Me	6-NH ₂	Me	OH
787	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	H	Me
788	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	H	NH ₂
789	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	H	OH
790	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	Me	Me
791	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	Me	NH ₂
792	CH ₂ CH ₂ Ph	OH	Me	7-NH ₂	Me	OH
793	CH ₂ CH ₂ Ph	OH	Me	5-Me	H	Me
794	CH ₂ CH ₂ Ph	OH	Me	5-Me	H	NH ₂
795	CH ₂ CH ₂ Ph	OH	Me	5-Me	H	OH
796	CH ₂ CH ₂ Ph	OH	Me	5-Me	Me	Me
797	CH ₂ CH ₂ Ph	OH	Me	5-Me	Me	NH ₂
798	CH ₂ CH ₂ Ph	OH	Me	5-Me	Me	OH
799	CH ₂ CH ₂ Ph	OH	Me	6-Me	H	Me
800	CH ₂ CH ₂ Ph	OH	Me	6-Me	H	NH ₂

TABLE 21

Compound No.	R1	R2	R3	R3'	R4	R5
801	CH ₂ CH ₂ Ph	OH	Me	6-Me	H	OH
802	CH ₂ CH ₂ Ph	OH	Me	6-Me	Me	Me
803	CH ₂ CH ₂ Ph	OH	Me	6-Me	Me	NH ₂
804	CH ₂ CH ₂ Ph	OH	Me	6-Me	Me	OH
805	CH ₂ CH ₂ Ph	OH	Me	7-Me	H	Me
806	CH ₂ CH ₂ Ph	OH	Me	7-Me	H	NH ₂
807	CH ₂ CH ₂ Ph	OH	Me	7-Me	H	OH
808	CH ₂ CH ₂ Ph	OH	Me	7-Me	Me	Me
809	CH ₂ CH ₂ Ph	OH	Me	7-Me	Me	NH ₂
810	CH ₂ CH ₂ Ph	OH	Me	7-Me	Me	OH
811	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	H	Me
812	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	H	NH ₂
813	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	H	OH
814	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	Me	Me
815	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	Me	NH ₂
816	CH ₂ CH ₂ Ph	OMe	Cl	5-Cl	Me	OH
817	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	H	Me
818	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	H	NH ₂
819	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	H	OH
820	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	Me	Me
821	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	Me	NH ₂
822	CH ₂ CH ₂ Ph	OMe	Cl	6-Cl	Me	OH
823	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	H	Me
824	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	H	NH ₂
825	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	H	OH
826	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	Me	Me
827	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	Me	NH ₂
828	CH ₂ CH ₂ Ph	OMe	Cl	7-Cl	Me	OH
829	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	H	Me

TABLE 21-continued

Compound No.	R1	R2	R3	R3'	R4	R5
830	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	H	NH ₂
831	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	H	OH
832	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	Me	Me
833	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	Me	NH ₂
834	CH ₂ CH ₂ Ph	OMe	Cl	5-NH ₂	Me	OH
835	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	H	Me
836	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	H	NH ₂
837	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	H	OH
838	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	Me	Me
839	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	Me	NH ₂
840	CH ₂ CH ₂ Ph	OMe	Cl	6-NH ₂	Me	OH

TABLE 22

Compound No.	R1	R2	R3	R3'	R4	R5
841	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	H	Me
842	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	H	NH ₂
843	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	H	OH
844	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	Me	Me
845	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	Me	NH ₂
846	CH ₂ CH ₂ Ph	OMe	Cl	7-NH ₂	Me	OH
847	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	H	Me
848	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	H	NH ₂
849	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	H	OH
850	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	Me	Me
851	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	Me	NH ₂
852	CH ₂ CH ₂ Ph	OMe	Cl	5-Me	Me	OH
853	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	H	Me
854	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	H	NH ₂
855	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	H	OH
856	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	Me	Me
857	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	Me	NH ₂
858	CH ₂ CH ₂ Ph	OMe	Cl	6-Me	Me	OH
859	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	H	Me
860	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	H	NH ₂
861	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	H	OH
862	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	Me	Me
863	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	Me	NH ₂
864	CH ₂ CH ₂ Ph	OMe	Cl	7-Me	Me	OH
865	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	H	Me
866	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	H	NH ₂
867	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	H	OH
868	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	Me	Me
869	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	Me	NH ₂
870	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Cl	Me	OH
871	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	H	Me
872	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	H	NH ₂
873	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	H	OH
874	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	Me	Me
875	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	Me	NH ₂
876	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Cl	Me	OH
877	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	H	Me
878	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	H	NH ₂
879	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	H	OH
880	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	Me	Me

TABLE 23

Compound No.	R1	R2	R3	R3'	R4	R5
881	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	Me	NH ₂
882	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Cl	Me	OH
883	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	H	Me
884	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	H	NH ₂
885	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	H	OH
886	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	Me	Me
887	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	Me	NH ₂
888	CH ₂ CH ₂ Ph	OMe	NH ₂	5-NH ₂	Me	OH
889	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	H	Me
890	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	H	NH ₂
891	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	H	OH

TABLE 23-continued

Compound No.	R1	R2	R3	R3'	R4	R5
892	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	Me	Me
893	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	Me	NH ₂
894	CH ₂ CH ₂ Ph	OMe	NH ₂	6-NH ₂	Me	OH
895	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	H	Me
896	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	H	NH ₂
897	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	H	OH
898	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	Me	Me
899	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	Me	NH ₂
900	CH ₂ CH ₂ Ph	OMe	NH ₂	7-NH ₂	Me	OH
901	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	H	Me
902	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	H	NH ₂
903	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	H	OH
904	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	Me	Me
905	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	Me	NH ₂
906	CH ₂ CH ₂ Ph	OMe	NH ₂	5-Me	Me	OH
907	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	H	Me
908	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	H	NH ₂
909	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	H	OH
910	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	Me	Me
911	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	Me	NH ₂
912	CH ₂ CH ₂ Ph	OMe	NH ₂	6-Me	Me	OH
913	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	H	Me
914	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	H	NH ₂
915	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	H	OH
916	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	Me	Me
917	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	Me	NH ₂
918	CH ₂ CH ₂ Ph	OMe	NH ₂	7-Me	Me	OH
919	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	H	Me
920	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	H	NH ₂

TABLE 24

Compound No.	R1	R2	R3	R3'	R4	R5
921	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	H	OH
922	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	Me	Me
923	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	Me	NH ₂
924	CH ₂ CH ₂ Ph	OMe	Me	5-Cl	Me	OH
925	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	H	Me
926	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	H	NH ₂
927	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	H	OH
928	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	Me	Me
929	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	Me	NH ₂
930	CH ₂ CH ₂ Ph	OMe	Me	6-Cl	Me	OH
931	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	H	Me
932	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	H	NH ₂
933	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	H	OH
934	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	Me	Me
935	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	Me	NH ₂
936	CH ₂ CH ₂ Ph	OMe	Me	7-Cl	Me	OH
937	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	H	Me
938	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	H	NH ₂
939	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	H	OH
940	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	Me	Me
941	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	Me	NH ₂
942	CH ₂ CH ₂ Ph	OMe	Me	5-NH ₂	Me	OH
943	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	H	Me
944	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	H	NH ₂
945	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	H	OH
946	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	Me	Me
947	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	Me	NH ₂
948	CH ₂ CH ₂ Ph	OMe	Me	6-NH ₂	Me	OH
949	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	H	Me
950	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	H	NH ₂
951	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	H	OH
952	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	Me	Me
953	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	Me	NH ₂
954	CH ₂ CH ₂ Ph	OMe	Me	7-NH ₂	Me	OH
955	CH ₂ CH ₂ Ph	OMe	Me	5-Me	H	Me
956	CH ₂ CH ₂ Ph	OMe	Me	5-Me	H	NH ₂
957	CH ₂ CH ₂ Ph	OMe	Me	5-Me	H	OH
958	CH ₂ CH ₂ Ph	OMe	Me	5-Me	Me	Me

TABLE 24-continued

Compound No.	R1	R2	R3	R3'	R4	R5
959	CH ₂ CH ₂ Ph	OMe	Me	5-Me	Me	NH ₂
960	CH ₂ CH ₂ Ph	OMe	Me	5-Me	Me	OH

TABLE 25

Compound No.	R1	R2	R3	R3'	R4	R5
961	CH ₂ CH ₂ Ph	OMe	Me	6-Me	H	Me
962	CH ₂ CH ₂ Ph	OMe	Me	6-Me	H	NH ₂
963	CH ₂ CH ₂ Ph	OMe	Me	6-Me	H	OH
964	CH ₂ CH ₂ Ph	OMe	Me	6-Me	Me	Me
965	CH ₂ CH ₂ Ph	OMe	Me	6-Me	Me	NH ₂
966	CH ₂ CH ₂ Ph	OMe	Me	6-Me	Me	OH
967	CH ₂ CH ₂ Ph	OMe	Me	7-Me	H	Me
968	CH ₂ CH ₂ Ph	OMe	Me	7-Me	H	NH ₂
969	CH ₂ CH ₂ Ph	OMe	Me	7-Me	H	OH
970	CH ₂ CH ₂ Ph	OMe	Me	7-Me	Me	Me
971	CH ₂ CH ₂ Ph	OMe	Me	7-Me	Me	NH ₂
972	CH ₂ CH ₂ Ph	OMe	Me	7-Me	Me	OH
973	H	H	Cl	5-H	H	Me
974	H	H	Cl	5-H	H	NH ₂
975	H	H	Cl	5-H	H	OH
976	H	H	Cl	5-H	Me	Me
977	H	H	Cl	5-H	Me	NH ₂
978	H	H	Cl	5-H	Me	OH
979	H	H	Cl	6-H	H	Me
980	H	H	Cl	6-H	H	NH ₂
981	H	H	Cl	6-H	H	OH
982	H	H	Cl	6-H	Me	Me
983	H	H	Cl	6-H	Me	NH ₂
984	H	H	Cl	6-H	Me	OH
985	H	H	Cl	7-H	H	Me
986	H	H	Cl	7-H	H	NH ₂
987	H	H	Cl	7-H	H	OH
988	H	H	Cl	7-H	Me	Me
989	H	H	Cl	7-H	Me	NH ₂
990	H	H	Cl	7-H	Me	OH
991	H	H	Cl	5-Cl	H	Me
992	H	H	Cl	5-Cl	H	NH ₂
993	H	H	Cl	5-Cl	H	OH
994	H	H	Cl	5-Cl	Me	Me
995	H	H	Cl	5-Cl	Me	NH ₂
996	H	H	Cl	5-Cl	Me	OH
997	H	H	Cl	6-Cl	H	Me
998	H	H	Cl	6-Cl	H	NH ₂
999	H	H	Cl	6-Cl	H	OH
1000	H	H	Cl	6-Cl	Me	Me

TABLE 26

Compound No.	R1	R2	R3	R3'	R4	R5
1001	H	H	Cl	6-Cl	Me	NH ₂
1002	H	H	Cl	6-Cl	Me	OH
1003	H	H	Cl	7-Cl	H	Me
1004	H	H	Cl	7-Cl	H	NH ₂
1005	H	H	Cl	7-Cl	H	OH
1006	H	H	Cl	7-Cl	Me	Me
1007	H	H	Cl	7-Cl	Me	NH ₂
1008	H	H	Cl	7-Cl	Me	OH
1009	H	H	Cl	5-NH ₂	H	Me
1010	H	H	Cl	5-NH ₂	H	NH ₂
1011	H	H	Cl	5-NH ₂	H	OH
1012	H	H	Cl	5-NH ₂	Me	Me
1013	H	H	Cl	5-NH ₂	Me	NH ₂
1014	H	H	Cl	5-NH ₂	Me	OH
1015	H	H	Cl	6-NH ₂	H	Me
1016	H	H	Cl	6-NH ₂	H	NH ₂
1017	H	H	Cl	6-NH ₂	H	OH
1018	H	H	Cl	6-NH ₂	Me	Me
1019	H	H	Cl	6-NH ₂	Me	NH ₂
1020	H	H	Cl	6-NH ₂	Me	OH

TABLE 26-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1021	H	H	Cl	7-NH2	H	Me
1022	H	H	Cl	7-NH2	H	NH2
1023	H	H	Cl	7-NH2	H	OH
1024	H	H	Cl	7-NH2	Me	Me
1025	H	H	Cl	7-NH2	Me	NH2
1026	H	H	Cl	7-NH2	Me	OH
1027	H	H	Cl	5-Me	H	Me
1028	H	H	Cl	5-Me	H	NH2
1029	H	H	Cl	5-Me	H	OH
1030	H	H	Cl	5-Me	Me	Me
1031	H	H	Cl	5-Me	Me	NH2
1032	H	H	Cl	5-Me	Me	OH
1033	H	H	Cl	6-Me	H	Me
1034	H	H	Cl	6-Me	H	NH2
1035	H	H	Cl	6-Me	H	OH
1036	H	H	Cl	6-Me	Me	Me
1037	H	H	Cl	6-Me	Me	NH2
1038	H	H	Cl	6-Me	Me	OH
1039	H	H	Cl	7-Me	H	Me
1040	H	H	Cl	7-Me	H	NH2

TABLE 27

Compound No.	R1	R2	R3	R3'	R4	R5
1041	H	H	Cl	7-Me	H	OH
1042	H	H	Cl	7-Me	Me	Me
1043	H	H	Cl	7-Me	Me	NH2
1044	H	H	Cl	7-Me	Me	OH
1045	H	H	NH2	5-H	H	Me
1046	H	H	NH2	5-H	H	NH2
1047	H	H	NH2	5-H	H	OH
1048	H	H	NH2	5-H	Me	Me
1049	H	H	NH2	5-H	Me	NH2
1050	H	H	NH2	5-H	Me	OH
1051	H	H	NH2	6-H	H	Me
1052	H	H	NH2	6-H	H	NH2
1053	H	H	NH2	6-H	H	OH
1054	H	H	NH2	6-H	Me	Me
1055	H	H	NH2	6-H	Me	NH2
1056	H	H	NH2	6-H	Me	OH
1057	H	H	NH2	7-H	H	Me
1058	H	H	NH2	7-H	H	NH2
1059	H	H	NH2	7-H	H	OH
1060	H	H	NH2	7-H	Me	Me
1061	H	H	NH2	7-H	Me	NH2
1062	H	H	NH2	7-H	Me	OH
1063	H	H	NH2	5-Cl	H	Me
1064	H	H	NH2	5-Cl	H	NH2
1065	H	H	NH2	5-Cl	H	OH
1066	H	H	NH2	5-Cl	Me	Me
1067	H	H	NH2	5-Cl	Me	NH2
1068	H	H	NH2	5-Cl	Me	OH
1069	H	H	NH2	6-Cl	H	Me
1070	H	H	NH2	6-Cl	H	NH2
1071	H	H	NH2	6-Cl	H	OH
1072	H	H	NH2	6-Cl	Me	Me
1073	H	H	NH2	6-Cl	Me	NH2
1074	H	H	NH2	6-Cl	Me	OH
1075	H	H	NH2	7-Cl	H	Me
1076	H	H	NH2	7-Cl	H	NH2
1077	H	H	NH2	7-Cl	H	OH
1078	H	H	NH2	7-Cl	Me	Me
1079	H	H	NH2	7-Cl	Me	NH2
1080	H	H	NH2	7-Cl	Me	OH

TABLE 28

Compound No.	R1	R2	R3	R3'	R4	R5
1081	H	H	NH2	5-NH2	H	Me
1082	H	H	NH2	5-NH2	H	NH2

TABLE 28-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1083	H	H	NH2	5-NH2	H	OH
1084	H	H	NH2	5-NH2	Me	Me
1085	H	H	NH2	5-NH2	Me	NH2
1086	H	H	NH2	5-NH2	Me	OH
1087	H	H	NH2	6-NH2	H	Me
1088	H	H	NH2	6-NH2	H	NH2
1089	H	H	NH2	6-NH2	H	OH
1090	H	H	NH2	6-NH2	Me	Me
1091	H	H	NH2	6-NH2	Me	NH2
1092	H	H	NH2	6-NH2	Me	OH
1093	H	H	NH2	7-NH2	H	Me
1094	H	H	NH2	7-NH2	H	NH2
1095	H	H	NH2	7-NH2	H	OH
1096	H	H	NH2	7-NH2	Me	Me
1097	H	H	NH2	7-NH2	Me	NH2
1098	H	H	NH2	7-NH2	Me	OH
1099	H	H	NH2	5-Me	H	Me
1100	H	H	NH2	5-Me	H	NH2
1101	H	H	NH2	5-Me	H	OH
1102	H	H	NH2	5-Me	Me	Me
1103	H	H	NH2	5-Me	Me	NH2
1104	H	H	NH2	5-Me	Me	OH
1105	H	H	NH2	6-Me	H	Me
1106	H	H	NH2	6-Me	H	NH2
1107	H	H	NH2	6-Me	H	OH
1108	H	H	NH2	6-Me	Me	Me
1109	H	H	NH2	6-Me	Me	NH2
1110	H	H	NH2	6-Me	Me	OH
1111	H	H	NH2	7-Me	H	Me
1112	H	H	NH2	7-Me	H	NH2
1113	H	H	NH2	7-Me	H	OH
1114	H	H	NH2	7-Me	Me	Me
1115	H	H	NH2	7-Me	Me	NH2
1116	H	H	NH2	7-Me	Me	OH
1117	H	H	Me	5-H	H	Me
1118	H	H	Me	5-H	H	NH2
1119	H	H	Me	5-H	H	OH
1120	H	H	Me	5-H	Me	Me

TABLE 29

Compound No.	R1	R2	R3	R3'	R4	R5
1121	H	H	Me	5-H	Me	NH2
1122	H	H	Me	5-H	Me	OH
1123	H	H	Me	6-H	H	Me
1124	H	H	Me	6-H	H	NH2
1125	H	H	Me	6-H	H	OH
1126	H	H	Me	6-H	Me	Me
1127	H	H	Me	6-H	Me	NH2
1128	H	H	Me	6-H	Me	OH
1129	H	H	Me	7-H	H	Me
1130	H	H	Me	7-H	H	NH2
1131	H	H	Me	7-H	H	OH
1132	H	H	Me	7-H	Me	Me
1133	H	H	Me	7-H	Me	NH2
1134	H	H	Me	7-H	Me	OH
1135	H	H	Me	5-Cl	H	Me
1136	H	H	Me	5-Cl	H	NH2
1137	H	H	Me	5-Cl	H	OH
1138	H	H	Me	5-Cl	Me	Me
1139	H	H	Me	5-Cl	Me	NH2
1140	H	H	Me	5-Cl	Me	OH
1141	H	H	Me	6-Cl	H	Me
1142	H	H	Me	6-Cl	H	NH2
1143	H	H	Me	6-Cl	H	OH
1144	H	H	Me	6-Cl	Me	Me
1145	H	H	Me	6-Cl	Me	NH2
1146	H	H	Me	6-Cl	Me	OH
1147	H	H	Me	7-Cl	H	Me
1148	H	H	Me	7-Cl	H	NH2
1149	H	H	Me	7-Cl	H	OH
1150	H	H	Me	7-Cl	Me	Me
1151	H	H	Me	7-Cl	Me	NH2

TABLE 29-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1152	H	H	Me	7-Cl	Me	OH
1153	H	H	Me	5-NH2	H	Me
1154	H	H	Me	5-NH2	H	NH2
1155	H	H	Me	5-NH2	H	OH
1156	H	H	Me	5-NH2	Me	Me
1157	H	H	Me	5-NH2	Me	NH2
1158	H	H	Me	5-NH2	Me	OH
1159	H	H	Me	6-NH2	H	Me
1160	H	H	Me	6-NH2	H	NH2

TABLE 30

Compound No.	R1	R2	R3	R3'	R4	R5
1161	H	H	Me	6-NH2	H	OH
1162	H	H	Me	6-NH2	Me	Me
1163	H	H	Me	6-NH2	Me	NH2
1164	H	H	Me	6-NH2	Me	OH
1165	H	H	Me	7-NH2	H	Me
1166	H	H	Me	7-NH2	H	NH2
1167	H	H	Me	7-NH2	H	OH
1168	H	H	Me	7-NH2	Me	Me
1169	H	H	Me	7-NH2	Me	NH2
1170	H	H	Me	7-NH2	Me	OH
1171	H	H	Me	5-Me	H	Me
1172	H	H	Me	5-Me	H	NH2
1173	H	H	Me	5-Me	H	OH
1174	H	H	Me	5-Me	Me	Me
1175	H	H	Me	5-Me	Me	NH2
1176	H	H	Me	5-Me	Me	OH
1177	H	H	Me	6-Me	H	Me
1178	H	H	Me	6-Me	H	NH2
1179	H	H	Me	6-Me	H	OH
1180	H	H	Me	6-Me	Me	Me
1181	H	H	Me	6-Me	Me	NH2
1182	H	H	Me	6-Me	Me	OH
1183	H	H	Me	7-Me	H	Me
1184	H	H	Me	7-Me	H	NH2
1185	H	H	Me	7-Me	H	OH
1186	H	H	Me	7-Me	Me	Me
1187	H	H	Me	7-Me	Me	NH2
1188	H	H	Me	7-Me	Me	OH
1189	H	H	H	5-Cl	H	Me
1190	H	H	H	5-Cl	H	NH2
1191	H	H	H	5-Cl	H	OH
1192	H	H	H	5-Cl	Me	Me
1193	H	H	H	5-Cl	Me	NH2
1194	H	H	H	5-Cl	Me	OH
1195	H	H	H	6-Cl	H	Me
1196	H	H	H	6-Cl	H	NH2
1197	H	H	H	6-Cl	H	OH
1198	H	H	H	6-Cl	Me	Me
1199	H	H	H	6-Cl	Me	NH2
1200	H	H	H	6-Cl	Me	OH

TABLE 31

Compound No.	R1	R2	R3	R3'	R4	R5
1201	H	H	H	7-Cl	H	Me
1202	H	H	H	7-Cl	H	NH2
1203	H	H	H	7-Cl	H	OH
1204	H	H	H	7-Cl	Me	Me
1205	H	H	H	7-Cl	Me	NH2
1206	H	H	H	7-Cl	Me	OH
1207	H	H	H	5-NH2	H	Me
1208	H	H	H	5-NH2	H	NH2
1209	H	H	H	5-NH2	H	OH
1210	H	H	H	5-NH2	Me	Me
1211	H	H	H	5-NH2	Me	NH2
1212	H	H	H	5-NH2	Me	OH
1213	H	H	H	6-NH2	H	Me

TABLE 31-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1214	H	H	H	6-NH2	H	NH2
1215	H	H	H	6-NH2	H	OH
1216	H	H	H	6-NH2	Me	Me
1217	H	H	H	6-NH2	Me	NH2
1218	H	H	H	6-NH2	Me	OH
1219	H	H	H	7-NH2	H	Me
1220	H	H	H	7-NH2	H	NH2
1221	H	H	H	7-NH2	H	OH
1222	H	H	H	7-NH2	Me	Me
1223	H	H	H	7-NH2	Me	NH2
1224	H	H	H	7-NH2	Me	OH
1225	H	H	H	5-Me	H	Me
1226	H	H	H	5-Me	H	NH2
1227	H	H	H	5-Me	H	OH
1228	H	H	H	5-Me	Me	Me
1229	H	H	H	5-Me	Me	NH2
1230	H	H	H	5-Me	Me	OH
1231	H	H	H	6-Me	H	Me
1232	H	H	H	6-Me	H	NH2
1233	H	H	H	6-Me	H	OH
1234	H	H	H	6-Me	Me	Me
1235	H	H	H	6-Me	Me	NH2
1236	H	H	H	6-Me	Me	OH
1237	H	H	H	7-Me	H	Me
1238	H	H	H	7-Me	H	NH2
1239	H	H	H	7-Me	H	OH
1240	H	H	H	7-Me	Me	Me

TABLE 32

Compound No.	R1	R2	R3	R3'	R4	R5
1241	H	H	H	7-Me	Me	NH2
1242	H	H	H	7-Me	Me	OH
1243	H	OMe	Cl	5-H	H	Me
1244	H	OMe	Cl	5-H	H	NH2
1245	H	OMe	Cl	5-H	H	OH
1246	H	OMe	Cl	5-H	Me	Me
1247	H	OMe	Cl	5-H	Me	NH2
1248	H	OMe	Cl	5-H	Me	OH
1249	H	OMe	Cl	6-H	H	Me
1250	H	OMe	Cl	6-H	H	NH2
1251	H	OMe	Cl	6-H	H	OH
1252	H	OMe	Cl	6-H	Me	Me
1253	H	OMe	Cl	6-H	Me	NH2
1254	H	OMe	Cl	6-H	Me	OH
1255	H	OMe	Cl	7-H	H	Me
1256	H	OMe	Cl	7-H	H	NH2
1257	H	OMe	Cl	7-H	H	OH
1258	H	OMe	Cl	7-H	Me	Me
1259	H	OMe	Cl	7-H	Me	NH2
1260	H	OMe	Cl	7-H	Me	OH
1261	H	OMe	Cl	5-Cl	H	Me
1262	H	OMe	Cl	5-Cl	H	NH2
1263	H	OMe	Cl	5-Cl	H	OH
1264	H	OMe	Cl	5-Cl	Me	Me
1265	H	OMe	Cl	5-Cl	Me	NH2
1266	H	OMe	Cl	5-Cl	Me	OH
1267	H	OMe	Cl	6-Cl	H	Me
1268	H	OMe	Cl	6-Cl	H	NH2
1269	H	OMe	Cl	6-Cl	H	OH
1270	H	OMe	Cl	6-Cl	Me	Me
1271	H	OMe	Cl	6-Cl	Me	NH2
1272	H	OMe	Cl	6-Cl	Me	OH
1273	H	OMe	Cl	7-Cl	H	Me
1274	H	OMe	Cl	7-Cl	H	NH2
1275	H	OMe	Cl	7-Cl	H	OH
1276	H	OMe	Cl	7-Cl	Me	Me
1277	H	OMe	Cl	7-Cl	Me	NH2
1278	H	OMe	Cl	7-Cl	Me	OH
1279	H	OMe	Cl	5-NH2	H	Me
1280	H	OMe	Cl	5-NH2	H	NH2

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TABLE 33

Compound No.	R1	R2	R3	R3'	R4	R5
1281	H	OMe	Cl	5-NH2	H	OH
1282	H	OMe	Cl	5-NH2	Me	Me
1283	H	OMe	Cl	5-NH2	Me	NH2
1284	H	OMe	Cl	5-NH2	Me	OH
1285	H	OMe	Cl	6-NH2	H	Me
1286	H	OMe	Cl	6-NH2	H	NH2
1287	H	OMe	Cl	6-NH2	H	OH
1288	H	OMe	Cl	6-NH2	Me	Me
1289	H	OMe	Cl	6-NH2	Me	NH2
1290	H	OMe	Cl	6-NH2	Me	OH
1291	H	OMe	Cl	7-NH2	H	Me
1292	H	OMe	Cl	7-NH2	H	NH2
1293	H	OMe	Cl	7-NH2	H	OH
1294	H	OMe	Cl	7-NH2	Me	Me
1295	H	OMe	Cl	7-NH2	Me	NH2
1296	H	OMe	Cl	7-NH2	Me	OH
1297	H	OMe	Cl	5-Me	H	Me
1298	H	OMe	Cl	5-Me	H	NH2
1299	H	OMe	Cl	5-Me	H	OH
1300	H	OMe	Cl	5-Me	Me	Me
1301	H	OMe	Cl	5-Me	Me	NH2
1302	H	OMe	Cl	5-Me	Me	OH
1303	H	OMe	Cl	6-Me	H	Me
1304	H	OMe	Cl	6-Me	H	NH2
1305	H	OMe	Cl	6-Me	H	OH
1306	H	OMe	Cl	6-Me	Me	Me
1307	H	OMe	Cl	6-Me	Me	NH2
1308	H	OMe	Cl	6-Me	Me	OH
1309	H	OMe	Cl	7-Me	H	Me
1310	H	OMe	Cl	7-Me	H	NH2
1311	H	OMe	Cl	7-Me	H	OH
1312	H	OMe	Cl	7-Me	Me	Me
1313	H	OMe	Cl	7-Me	Me	NH2
1314	H	OMe	Cl	7-Me	Me	OH
1315	H	OMe	NH2	5-H	H	Me
1316	H	OMe	NH2	5-H	H	NH2
1317	H	OMe	NH2	5-H	H	OH
1318	H	OMe	NH2	5-H	Me	Me
1319	H	OMe	NH2	5-H	Me	NH2
1320	H	OMe	NH2	5-H	Me	OH

TABLE 34

Compound No.	R1	R2	R3	R3'	R4	R5
1321	H	OMe	NH2	6-H	H	Me
1322	H	OMe	NH2	6-H	H	NH2
1323	H	OMe	NH2	6-H	H	OH
1324	H	OMe	NH2	6-H	Me	Me
1325	H	OMe	NH2	6-H	Me	NH2
1326	H	OMe	NH2	6-H	Me	OH
1327	H	OMe	NH2	7-H	H	Me
1328	H	OMe	NH2	7-H	H	NH2
1329	H	OMe	NH2	7-H	H	OH
1330	H	OMe	NH2	7-H	Me	Me
1331	H	OMe	NH2	7-H	Me	NH2
1332	H	OMe	NH2	7-H	Me	OH
1333	H	OMe	NH2	5-Cl	H	Me
1334	H	OMe	NH2	5-Cl	H	NH2
1335	H	OMe	NH2	5-Cl	H	OH
1336	H	OMe	NH2	5-Cl	Me	Me
1337	H	OMe	NH2	5-Cl	Me	NH2
1338	H	OMe	NH2	5-Cl	Me	OH
1339	H	OMe	NH2	6-Cl	H	Me
1340	H	OMe	NH2	6-Cl	H	NH2
1341	H	OMe	NH2	6-Cl	H	OH
1342	H	OMe	NH2	6-Cl	Me	Me
1343	H	OMe	NH2	6-Cl	Me	NH2
1344	H	OMe	NH2	6-Cl	Me	OH
1345	H	OMe	NH2	7-Cl	H	Me
1346	H	OMe	NH2	7-Cl	H	NH2
1347	H	OMe	NH2	7-Cl	H	OH
1348	H	OMe	NH2	7-Cl	Me	Me
1349	H	OMe	NH2	7-Cl	Me	NH2

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TABLE 34-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1350	H	OMe	NH2	7-Cl	Me	OH
1351	H	OMe	NH2	5-NH2	H	Me
1352	H	OMe	NH2	5-NH2	H	NH2
1353	H	OMe	NH2	5-NH2	H	OH
1354	H	OMe	NH2	5-NH2	Me	Me
1355	H	OMe	NH2	5-NH2	Me	NH2
1356	H	OMe	NH2	5-NH2	Me	OH
1357	H	OMe	NH2	6-NH2	H	Me
1358	H	OMe	NH2	6-NH2	H	NH2
1359	H	OMe	NH2	6-NH2	H	OH
1360	H	OMe	NH2	6-NH2	Me	Me

TABLE 35

Compound No.	R1	R2	R3	R3'	R4	R5
1361	H	OMe	NH2	6-NH2	Me	NH2
1362	H	OMe	NH2	6-NH2	Me	OH
1363	H	OMe	NH2	7-NH2	H	Me
1364	H	OMe	NH2	7-NH2	H	NH2
1365	H	OMe	NH2	7-NH2	H	OH
1366	H	OMe	NH2	7-NH2	Me	Me
1367	H	OMe	NH2	7-NH2	Me	NH2
1368	H	OMe	NH2	7-NH2	Me	OH
1369	H	OMe	NH2	5-Me	H	Me
1370	H	OMe	NH2	5-Me	H	NH2
1371	H	OMe	NH2	5-Me	H	OH
1372	H	OMe	NH2	5-Me	Me	Me
1373	H	OMe	NH2	5-Me	Me	NH2
1374	H	OMe	NH2	5-Me	Me	OH
1375	H	OMe	NH2	6-Me	H	Me
1376	H	OMe	NH2	6-Me	H	NH2
1377	H	OMe	NH2	6-Me	H	OH
1378	H	OMe	NH2	6-Me	Me	Me
1379	H	OMe	NH2	6-Me	Me	NH2
1380	H	OMe	NH2	6-Me	Me	OH
1381	H	OMe	NH2	7-Me	H	Me
1382	H	OMe	NH2	7-Me	H	NH2
1383	H	OMe	NH2	7-Me	H	OH
1384	H	OMe	NH2	7-Me	Me	Me
1385	H	OMe	NH2	7-Me	Me	NH2
1386	H	OMe	NH2	7-Me	Me	OH
1387	H	OMe	Me	5-H	H	Me
1388	H	OMe	Me	5-H	H	NH2
1389	H	OMe	Me	5-H	H	OH
1390	H	OMe	Me	5-H	Me	Me
1391	H	OMe	Me	5-H	Me	NH2
1392	H	OMe	Me	5-H	Me	OH
1393	H	OMe	Me	6-H	H	Me
1394	H	OMe	Me	6-H	H	NH2
1395	H	OMe	Me	6-H	H	OH
1396	H	OMe	Me	6-H	Me	Me
1397	H	OMe	Me	6-H	Me	NH2
1398	H	OMe	Me	6-H	Me	OH
1399	H	OMe	Me	7-H	H	Me
1400	H	OMe	Me	7-H	H	NH2

TABLE 36

Compound No.	R1	R2	R3	R3'	R4	R5
1401	H	OMe	Me	7-H	H	OH
1402	H	OMe	Me	7-H	Me	Me
1403	H	OMe	Me	7-H	Me	NH2
1404	H	OMe	Me	7-H	Me	OH
1405	H	OMe	Me	5-Cl	H	Me
1406	H	OMe	Me	5-Cl	H	NH2
1407	H	OMe	Me	5-Cl	H	OH
1408	H	OMe	Me	5-Cl	Me	Me
1409	H	OMe	Me	5-Cl	Me	NH2
1410	H	OMe	Me	5-Cl	Me	OH
1411	H	OMe	Me	6-Cl	H	Me

TABLE 36-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1412	H	OMe	Me	6-Cl	H	NH2
1413	H	OMe	Me	6-Cl	H	OH
1414	H	OMe	Me	6-Cl	Me	Me
1415	H	OMe	Me	6-Cl	Me	NH2
1416	H	OMe	Me	6-Cl	Me	OH
1417	H	OMe	Me	7-Cl	H	Me
1418	H	OMe	Me	7-Cl	H	NH2
1419	H	OMe	Me	7-Cl	H	OH
1420	H	OMe	Me	7-Cl	Me	Me
1421	H	OMe	Me	7-Cl	Me	NH2
1422	H	OMe	Me	7-Cl	Me	OH
1423	H	OMe	Me	5-NH2	H	Me
1424	H	OMe	Me	5-NH2	H	NH2
1425	H	OMe	Me	5-NH2	H	OH
1426	H	OMe	Me	5-NH2	Me	Me
1427	H	OMe	Me	5-NH2	Me	NH2
1428	H	OMe	Me	5-NH2	Me	OH
1429	H	OMe	Me	6-NH2	H	Me
1430	H	OMe	Me	6-NH2	H	NH2
1431	H	OMe	Me	6-NH2	H	OH
1432	H	OMe	Me	6-NH2	Me	Me
1433	H	OMe	Me	6-NH2	Me	NH2
1434	H	OMe	Me	6-NH2	Me	OH
1435	H	OMe	Me	7-NH2	H	Me
1436	H	OMe	Me	7-NH2	H	NH2
1437	H	OMe	Me	7-NH2	H	OH
1438	H	OMe	Me	7-NH2	Me	Me
1439	H	OMe	Me	7-NH2	Me	NH2
1440	H	OMe	Me	7-NH2	Me	OH

TABLE 37

Compound No.	R1	R2	R3	R3'	R4	R5
1441	H	OMe	Me	5-Me	H	Me
1442	H	OMe	Me	5-Me	H	NH2
1443	H	OMe	Me	5-Me	H	OH
1444	H	OMe	Me	5-Me	Me	Me
1445	H	OMe	Me	5-Me	Me	NH2
1446	H	OMe	Me	5-Me	Me	OH
1447	H	OMe	Me	6-Me	H	Me
1448	H	OMe	Me	6-Me	H	NH2
1449	H	OMe	Me	6-Me	H	OH
1450	H	OMe	Me	6-Me	Me	Me
1451	H	OMe	Me	6-Me	Me	NH2
1452	H	OMe	Me	6-Me	Me	OH
1453	H	OMe	Me	7-Me	H	Me
1454	H	OMe	Me	7-Me	H	NH2
1455	H	OMe	Me	7-Me	H	OH
1456	H	OMe	Me	7-Me	Me	Me
1457	H	OMe	Me	7-Me	Me	NH2
1458	H	OMe	Me	7-Me	Me	OH
1459	H	OMe	H	5-Cl	H	Me
1460	H	OMe	H	5-Cl	H	NH2
1461	H	OMe	H	5-Cl	H	OH
1462	H	OMe	H	5-Cl	Me	Me
1463	H	OMe	H	5-Cl	Me	NH2
1464	H	OMe	H	5-Cl	Me	OH
1465	H	OMe	H	6-Cl	H	Me
1466	H	OMe	H	6-Cl	H	NH2
1467	H	OMe	H	6-Cl	H	OH
1468	H	OMe	H	6-Cl	Me	Me
1469	H	OMe	H	6-Cl	Me	NH2
1470	H	OMe	H	6-Cl	Me	OH
1471	H	OMe	H	7-Cl	H	Me
1472	H	OMe	H	7-Cl	H	NH2
1473	H	OMe	H	7-Cl	H	OH
1474	H	OMe	H	7-Cl	Me	Me
1475	H	OMe	H	7-Cl	Me	NH2
1476	H	OMe	H	7-Cl	Me	OH
1477	H	OMe	H	5-NH2	H	Me
1478	H	OMe	H	5-NH2	H	NH2

TABLE 37-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1479	H	OMe	H	5-NH2	H	OH
1480	H	OMe	H	5-NH2	Me	Me

TABLE 38

Compound No.	R1	R2	R3	R3'	R4	R5
1481	H	OMe	H	5-NH2	Me	NH2
1482	H	OMe	H	5-NH2	Me	OH
1483	H	OMe	H	6-NH2	H	Me
1484	H	OMe	H	6-NH2	H	NH2
1485	H	OMe	H	6-NH2	H	OH
1486	H	OMe	H	6-NH2	Me	Me
1487	H	OMe	H	6-NH2	Me	NH2
1488	H	OMe	H	6-NH2	Me	OH
1489	H	OMe	H	7-NH2	H	Me
1490	H	OMe	H	7-NH2	H	NH2
1491	H	OMe	H	7-NH2	H	OH
1492	H	OMe	H	7-NH2	Me	Me
1493	H	OMe	H	7-NH2	Me	NH2
1494	H	OMe	H	7-NH2	Me	OH
1495	H	OMe	H	5-Me	H	Me
1496	H	OMe	H	5-Me	H	NH2
1497	H	OMe	H	5-Me	H	OH
1498	H	OMe	H	5-Me	Me	Me
1499	H	OMe	H	5-Me	Me	NH2
1500	H	OMe	H	5-Me	Me	OH
1501	H	OMe	H	6-Me	H	Me
1502	H	OMe	H	6-Me	H	NH2
1503	H	OMe	H	6-Me	H	OH
1504	H	OMe	H	6-Me	Me	Me
1505	H	OMe	H	6-Me	Me	NH2
1506	H	OMe	H	6-Me	Me	OH
1507	H	OMe	H	7-Me	H	Me
1508	H	OMe	H	7-Me	H	NH2
1509	H	OMe	H	7-Me	H	OH
1510	H	OMe	H	7-Me	Me	Me
1511	H	OMe	H	7-Me	Me	NH2
1512	H	OMe	H	7-Me	Me	OH
1513	2-thienylethyl	H	Cl	5-H	H	Me
1514	2-thienylethyl	H	Cl	5-H	H	NH2
1515	2-thienylethyl	H	Cl	5-H	H	OH
1516	2-thienylethyl	H	Cl	5-H	Me	Me
1517	2-thienylethyl	H	Cl	5-H	Me	NH2
1518	2-thienylethyl	H	Cl	5-H	Me	OH
1519	2-thienylethyl	H	Cl	6-H	H	Me
1520	2-thienylethyl	H	Cl	6-H	H	NH2

TABLE 39

Compound No.	R1	R2	R3	R3'	R4	R5
1521	2-thienylethyl	H	Cl	6-H	H	OH
1522	2-thienylethyl	H	Cl	6-H	Me	Me
1523	2-thienylethyl	H	Cl	6-H	Me	NH2
1524	2-thienylethyl	H	Cl	6-H	Me	OH
1525	2-thienylethyl	H	Cl	7-H	H	Me
1526	2-thienylethyl	H	Cl	7-H	H	NH2
1527	2-thienylethyl	H	Cl	7-H	H	OH
1528	2-thienylethyl	H	Cl	7-H	Me	Me
1529	2-thienylethyl	H	Cl	7-H	Me	NH2
1530	2-thienylethyl	H	Cl	7-H	Me	OH
1531	2-thienylethyl	H	Cl	5-Cl	H	Me
1532	2-thienylethyl	H	Cl	5-Cl	H	NH2
1533	2-thienylethyl	H	Cl	5-Cl	H	OH
1534	2-thienylethyl	H	Cl	5-Cl	Me	Me
1535	2-thienylethyl	H	Cl	5-Cl	Me	NH2
1536	2-thienylethyl	H	Cl	5-Cl	Me	OH
1537	2-thienylethyl	H	Cl	6-Cl	H	Me
1538	2-thienylethyl	H	Cl	6-Cl	H	NH2
1539	2-thienylethyl	H	Cl	6-Cl	H	OH
1540	2-thienylethyl	H	Cl	6-Cl	Me	Me

TABLE 39-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1541	2-thienylethyl	H	Cl	6-Cl	Me	NH2
1542	2-thienylethyl	H	Cl	6-Cl	Me	OH
1543	2-thienylethyl	H	Cl	7-Cl	H	Me
1544	2-thienylethyl	H	Cl	7-Cl	H	NH2
1545	2-thienylethyl	H	Cl	7-Cl	H	OH
1546	2-thienylethyl	H	Cl	7-Cl	Me	Me
1547	2-thienylethyl	H	Cl	7-Cl	Me	NH2
1548	2-thienylethyl	H	Cl	7-Cl	Me	OH
1549	2-thienylethyl	H	Cl	5-NH2	H	Me
1550	2-thienylethyl	H	Cl	5-NH2	H	NH2
1551	2-thienylethyl	H	Cl	5-NH2	H	OH
1552	2-thienylethyl	H	Cl	5-NH2	Me	Me
1553	2-thienylethyl	H	Cl	5-NH2	Me	NH2
1554	2-thienylethyl	H	Cl	5-NH2	Me	OH
1555	2-thienylethyl	H	Cl	6-NH2	H	Me
1556	2-thienylethyl	H	Cl	6-NH2	H	NH2
1557	2-thienylethyl	H	Cl	6-NH2	H	OH
1558	2-thienylethyl	H	Cl	6-NH2	Me	Me
1559	2-thienylethyl	H	Cl	6-NH2	Me	NH2
1560	2-thienylethyl	H	Cl	6-NH2	Me	OH

TABLE 40

Compound No.	R1	R2	R3	R3'	R4	R5
1561	2-thienylethyl	H	Cl	7-NH2	H	Me
1562	2-thienylethyl	H	Cl	7-NH2	H	NH2
1563	2-thienylethyl	H	Cl	7-NH2	H	OH
1564	2-thienylethyl	H	Cl	7-NH2	Me	Me
1565	2-thienylethyl	H	Cl	7-NH2	Me	NH2
1566	2-thienylethyl	H	Cl	7-NH2	Me	OH
1567	2-thienylethyl	H	Cl	5-Me	H	Me
1568	2-thienylethyl	H	Cl	5-Me	H	NH2
1569	2-thienylethyl	H	Cl	5-Me	H	OH
1570	2-thienylethyl	H	Cl	5-Me	Me	Me
1571	2-thienylethyl	H	Cl	5-Me	Me	NH2
1572	2-thienylethyl	H	Cl	5-Me	Me	OH
1573	2-thienylethyl	H	Cl	6-Me	H	Me
1574	2-thienylethyl	H	Cl	6-Me	H	NH2
1575	2-thienylethyl	H	Cl	6-Me	H	OH
1576	2-thienylethyl	H	Cl	6-Me	Me	Me
1577	2-thienylethyl	H	Cl	6-Me	Me	NH2
1578	2-thienylethyl	H	Cl	6-Me	Me	OH
1579	2-thienylethyl	H	Cl	7-Me	H	Me
1580	2-thienylethyl	H	Cl	7-Me	H	NH2
1581	2-thienylethyl	H	Cl	7-Me	H	OH
1582	2-thienylethyl	H	Cl	7-Me	Me	Me
1583	2-thienylethyl	H	Cl	7-Me	Me	NH2
1584	2-thienylethyl	H	Cl	7-Me	Me	OH
1585	2-thienylethyl	H	NH2	5-H	H	Me
1586	2-thienylethyl	H	NH2	5-H	H	NH2
1587	2-thienylethyl	H	NH2	5-H	H	OH
1588	2-thienylethyl	H	NH2	5-H	Me	Me
1589	2-thienylethyl	H	NH2	5-H	Me	NH2
1590	2-thienylethyl	H	NH2	5-H	Me	OH
1591	2-thienylethyl	H	NH2	6-H	H	Me
1592	2-thienylethyl	H	NH2	6-H	H	NH2
1593	2-thienylethyl	H	NH2	6-H	H	OH
1594	2-thienylethyl	H	NH2	6-H	Me	Me
1595	2-thienylethyl	H	NH2	6-H	Me	NH2
1596	2-thienylethyl	H	NH2	6-H	Me	OH
1597	2-thienylethyl	H	NH2	7-H	H	Me
1598	2-thienylethyl	H	NH2	7-H	H	NH2
1599	2-thienylethyl	H	NH2	7-H	H	OH
1600	2-thienylethyl	H	NH2	7-H	Me	Me

TABLE 41

Compound No.	R1	R2	R3	R3'	R4	R5
1601	2-thienylethyl	H	NH2	7-H	Me	NH2
1602	2-thienylethyl	H	NH2	7-H	Me	OH

TABLE 41-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1603	2-thienylethyl	H	NH2	5-Cl	H	Me
1604	2-thienylethyl	H	NH2	5-Cl	H	NH2
1605	2-thienylethyl	H	NH2	5-Cl	H	OH
1606	2-thienylethyl	H	NH2	5-Cl	Me	Me
1607	2-thienylethyl	H	NH2	5-Cl	Me	NH2
1608	2-thienylethyl	H	NH2	5-Cl	Me	OH
1609	2-thienylethyl	H	NH2	6-Cl	H	Me
1610	2-thienylethyl	H	NH2	6-Cl	H	NH2
1611	2-thienylethyl	H	NH2	6-Cl	H	OH
1612	2-thienylethyl	H	NH2	6-Cl	Me	Me
1613	2-thienylethyl	H	NH2	6-Cl	Me	NH2
1614	2-thienylethyl	H	NH2	6-Cl	Me	OH
1615	2-thienylethyl	H	NH2	7-Cl	H	Me
1616	2-thienylethyl	H	NH2	7-Cl	H	NH2
1617	2-thienylethyl	H	NH2	7-Cl	H	OH
1618	2-thienylethyl	H	NH2	7-Cl	Me	Me
1619	2-thienylethyl	H	NH2	7-Cl	Me	NH2
1620	2-thienylethyl	H	NH2	7-Cl	Me	OH
1621	2-thienylethyl	H	NH2	5-NH2	H	Me
1622	2-thienylethyl	H	NH2	5-NH2	H	NH2
1623	2-thienylethyl	H	NH2	5-NH2	H	OH
1624	2-thienylethyl	H	NH2	5-NH2	Me	Me
1625	2-thienylethyl	H	NH2	5-NH2	Me	NH2
1626	2-thienylethyl	H	NH2	5-NH2	Me	OH
1627	2-thienylethyl	H	NH2	6-NH2	H	Me
1628	2-thienylethyl	H	NH2	6-NH2	H	NH2
1629	2-thienylethyl	H	NH2	6-NH2	H	OH
1630	2-thienylethyl	H	NH2	6-NH2	Me	Me
1631	2-thienylethyl	H	NH2	6-NH2	Me	NH2
1632	2-thienylethyl	H	NH2	6-NH2	Me	OH
1633	2-thienylethyl	H	NH2	7-NH2	H	Me
1634	2-thienylethyl	H	NH2	7-NH2	H	NH2
1635	2-thienylethyl	H	NH2	7-NH2	H	OH
1636	2-thienylethyl	H	NH2	7-NH2	Me	Me
1637	2-thienylethyl	H	NH2	7-NH2	Me	NH2
1638	2-thienylethyl	H	NH2	7-NH2	Me	OH
1639	2-thienylethyl	H	NH2	5-Me	H	Me
1640	2-thienylethyl	H	NH2	5-Me	H	NH2

TABLE 42

Compound No.	R1	R2	R3	R3'	R4	R5
1641	2-thienylethyl	H	NH2	5-Me	H	OH
1642	2-thienylethyl	H	NH2	5-Me	Me	Me
1643	2-thienylethyl	H	NH2	5-Me	Me	NH2
1644	2-thienylethyl	H	NH2	5-Me	Me	OH
1645	2-thienylethyl	H	NH2	6-Me	H	Me
1646	2-thienylethyl	H	NH2	6-Me	H	NH2
1647	2-thienylethyl	H	NH2	6-Me	H	OH
1648	2-thienylethyl	H	NH2	6-Me	Me	Me
1649	2-thienylethyl	H	NH2	6-Me	Me	NH2
1650	2-thienylethyl	H	NH2	6-Me	Me	OH
1651	2-thienylethyl	H	NH2	7-Me	H	Me
1652	2-thienylethyl	H	NH2	7-Me	H	NH2
1653	2-thienylethyl	H	NH2	7-Me	H	OH
1654	2-thienylethyl	H	NH2	7-Me	Me	Me
1655	2-thienylethyl	H	NH2	7-Me	Me	NH2
1656	2-thienylethyl	H	NH2	7-Me	Me	OH
1657	2-thienylethyl	H	Me	5-H	H	Me
1658	2-thienylethyl	H	Me	5-H	H	NH2
1659	2-thienylethyl	H	Me	5-H	H	OH
1660	2-thienylethyl	H	Me	5-H	Me	Me
1661	2-thienylethyl	H	Me	5-H	Me	NH2
1662	2-thienylethyl	H	Me	5-H	Me	OH
1663	2-thienylethyl	H	Me	6-H	H	Me
1664	2-thienylethyl	H	Me	6-H	H	NH2
1665	2-thienylethyl	H	Me	6-H	H	OH
1666	2-thienylethyl	H	Me	6-H	Me	Me
1667	2-thienylethyl	H	Me	6-H	Me	NH2
1668	2-thienylethyl	H	Me	6-H	Me	OH
1669	2-thienylethyl	H	Me	7-H	H	Me
1670	2-thienylethyl	H	Me	7-H	H	NH2
1671	2-thienylethyl	H	Me	7-H	H	OH

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TABLE 42-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1672	2-thienylethyl	H	Me	7-H	Me	Me
1673	2-thienylethyl	H	Me	7-H	Me	NH2
1674	2-thienylethyl	H	Me	7-H	Me	OH
1675	2-thienylethyl	H	Me	5-Cl	H	Me
1676	2-thienylethyl	H	Me	5-Cl	H	NH2
1677	2-thienylethyl	H	Me	5-Cl	H	OH
1678	2-thienylethyl	H	Me	5-Cl	Me	Me
1679	2-thienylethyl	H	Me	5-Cl	Me	NH2
1680	2-thienylethyl	H	Me	5-Cl	Me	OH

TABLE 43

Compound No.	R1	R2	R3	R3'	R4	R5
1681	2-thienylethyl	H	Me	6-Cl	H	Me
1682	2-thienylethyl	H	Me	6-Cl	H	NH2
1683	2-thienylethyl	H	Me	6-Cl	H	OH
1684	2-thienylethyl	H	Me	6-Cl	Me	Me
1685	2-thienylethyl	H	Me	6-Cl	Me	NH2
1686	2-thienylethyl	H	Me	6-Cl	Me	OH
1687	2-thienylethyl	H	Me	7-Cl	H	Me
1688	2-thienylethyl	H	Me	7-Cl	H	NH2
1689	2-thienylethyl	H	Me	7-Cl	H	OH
1690	2-thienylethyl	H	Me	7-Cl	Me	Me
1691	2-thienylethyl	H	Me	7-Cl	Me	NH2
1692	2-thienylethyl	H	Me	7-Cl	Me	OH
1693	2-thienylethyl	H	Me	5-NH2	H	Me
1694	2-thienylethyl	H	Me	5-NH2	H	NH2
1695	2-thienylethyl	H	Me	5-NH2	H	OH
1696	2-thienylethyl	H	Me	5-NH2	Me	Me
1697	2-thienylethyl	H	Me	5-NH2	Me	NH2
1698	2-thienylethyl	H	Me	5-NH2	Me	OH
1699	2-thienylethyl	H	Me	6-NH2	H	Me
1700	2-thienylethyl	H	Me	6-NH2	H	NH2
1701	2-thienylethyl	H	Me	6-NH2	H	OH
1702	2-thienylethyl	H	Me	6-NH2	Me	Me
1703	2-thienylethyl	H	Me	6-NH2	Me	NH2
1704	2-thienylethyl	H	Me	6-NH2	Me	OH
1705	2-thienylethyl	H	Me	7-NH2	H	Me
1706	2-thienylethyl	H	Me	7-NH2	H	NH2
1707	2-thienylethyl	H	Me	7-NH2	H	OH
1708	2-thienylethyl	H	Me	7-NH2	Me	Me
1709	2-thienylethyl	H	Me	7-NH2	Me	NH2
1710	2-thienylethyl	H	Me	7-NH2	Me	OH
1711	2-thienylethyl	H	Me	5-Me	H	Me
1712	2-thienylethyl	H	Me	5-Me	H	NH2
1713	2-thienylethyl	H	Me	5-Me	H	OH
1714	2-thienylethyl	H	Me	5-Me	Me	Me
1715	2-thienylethyl	H	Me	5-Me	Me	NH2
1716	2-thienylethyl	H	Me	5-Me	Me	OH
1717	2-thienylethyl	H	Me	6-Me	H	Me
1718	2-thienylethyl	H	Me	6-Me	H	NH2
1719	2-thienylethyl	H	Me	6-Me	H	OH
1720	2-thienylethyl	H	Me	6-Me	Me	Me

TABLE 44

Compound No.	R1	R2	R3	R3'	R4	R5
1721	2-thienylethyl	H	Me	6-Me	Me	NH2
1722	2-thienylethyl	H	Me	6-Me	Me	OH
1723	2-thienylethyl	H	Me	7-Me	H	Me
1724	2-thienylethyl	H	Me	7-Me	H	NH2
1725	2-thienylethyl	H	Me	7-Me	H	OH
1726	2-thienylethyl	H	Me	7-Me	Me	Me
1727	2-thienylethyl	H	Me	7-Me	Me	NH2
1728	2-thienylethyl	H	Me	7-Me	Me	OH
1729	2-thienylethyl	H	H	5-Cl	H	Me
1730	2-thienylethyl	H	H	5-Cl	H	NH2
1731	2-thienylethyl	H	H	5-Cl	H	OH
1732	2-thienylethyl	H	H	5-Cl	Me	Me
1733	2-thienylethyl	H	H	5-Cl	Me	NH2

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TABLE 44-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1734	2-thienylethyl	H	H	5-Cl	Me	OH
1735	2-thienylethyl	H	H	6-Cl	H	Me
1736	2-thienylethyl	H	H	6-Cl	H	NH2
1737	2-thienylethyl	H	H	6-Cl	H	OH
1738	2-thienylethyl	H	H	6-Cl	Me	Me
1739	2-thienylethyl	H	H	6-Cl	Me	NH2
1740	2-thienylethyl	H	H	6-Cl	Me	OH
1741	2-thienylethyl	H	H	7-Cl	H	Me
1742	2-thienylethyl	H	H	7-Cl	H	NH2
1743	2-thienylethyl	H	H	7-Cl	H	OH
1744	2-thienylethyl	H	H	7-Cl	Me	Me
1745	2-thienylethyl	H	H	7-Cl	Me	NH2
1746	2-thienylethyl	H	H	7-Cl	Me	OH
1747	2-thienylethyl	H	H	5-NH2	H	Me
1748	2-thienylethyl	H	H	5-NH2	H	NH2
1749	2-thienylethyl	H	H	5-NH2	H	OH
1750	2-thienylethyl	H	H	5-NH2	Me	Me
1751	2-thienylethyl	H	H	5-NH2	Me	NH2
1752	2-thienylethyl	H	H	5-NH2	Me	OH
1753	2-thienylethyl	H	H	6-NH2	H	Me
1754	2-thienylethyl	H	H	6-NH2	H	NH2
1755	2-thienylethyl	H	H	6-NH2	H	OH
1756	2-thienylethyl	H	H	6-NH2	Me	Me
1757	2-thienylethyl	H	H	6-NH2	Me	NH2
1758	2-thienylethyl	H	H	6-NH2	Me	OH
1759	2-thienylethyl	H	H	7-NH2	H	Me
1760	2-thienylethyl	H	H	7-NH2	H	NH2

TABLE 45

Compound No.	R1	R2	R3	R3'	R4	R5
1761	2-thienylethyl	H	H	7-NH2	H	OH
1762	2-thienylethyl	H	H	7-NH2	Me	Me
1763	2-thienylethyl	H	H	7-NH2	Me	NH2
1764	2-thienylethyl	H	H	7-NH2	Me	OH
1765	2-thienylethyl	H	H	5-Me	H	Me
1766	2-thienylethyl	H	H	5-Me	H	NH2
1767	2-thienylethyl	H	H	5-Me	H	OH
1768	2-thienylethyl	H	H	5-Me	Me	Me
1769	2-thienylethyl	H	H	5-Me	Me	NH2
1770	2-thienylethyl	H	H	5-Me	Me	OH
1771	2-thienylethyl	H	H	6-Me	H	Me
1772	2-thienylethyl	H	H	6-Me	H	NH2
1773	2-thienylethyl	H	H	6-Me	H	OH
1774	2-thienylethyl	H	H	6-Me	Me	Me
1775	2-thienylethyl	H	H	6-Me	Me	NH2
1776	2-thienylethyl	H	H	6-Me	Me	OH
1777	2-thienylethyl	H	H	7-Me	H	Me
1778	2-thienylethyl	H	H	7-Me	H	NH2
1779	2-thienylethyl	H	H	7-Me	H	OH
1780	2-thienylethyl	H	H	7-Me	Me	Me
1781	2-thienylethyl	H	H	7-Me	Me	NH2
1782	2-thienylethyl	H	H	7-Me	Me	OH
1783	2-thienylethyl	OMe	Cl	5-H	H	Me
1784	2-thienylethyl	OMe	Cl	5-H	H	NH2
1785	2-thienylethyl	OMe	Cl	5-H	H	OH
1786	2-thienylethyl	OMe	Cl	5-H	Me	Me
1787	2-thienylethyl	OMe	Cl	5-H	Me	NH2
1788	2-thienylethyl	OMe	Cl	5-H	Me	OH
1789	2-thienylethyl	OMe	Cl	6-H	H	Me
1790	2-thienylethyl	OMe	Cl	6-H	H	NH2
1791	2-thienylethyl	OMe	Cl	6-H	H	OH
1792	2-thienylethyl	OMe	Cl	6-H	Me	Me
1793	2-thienylethyl	OMe	Cl	6-H	Me	NH2
1794	2-thienylethyl	OMe	Cl	6-H	Me	OH
1795	2-thienylethyl	OMe	Cl	7-H	H	Me
1796	2-thienylethyl	OMe	Cl	7-H	H	NH2
1797	2-thienylethyl	OMe	Cl	7-H	H	OH
1798	2-thienylethyl	OMe	Cl	7-H	Me	Me
1799	2-thienylethyl	OMe	Cl	7-H	Me	NH2
1800	2-thienylethyl	OMe	Cl	7-H	Me	OH

TABLE 46

Compound No.	R1	R2	R3	R3'	R4	R5
1801	2-thienylethyl	OMe	Cl	5-Cl	H	Me
1802	2-thienylethyl	OMe	Cl	5-Cl	H	NH2
1803	2-thienylethyl	OMe	Cl	5-Cl	H	OH
1804	2-thienylethyl	OMe	Cl	5-Cl	Me	Me
1805	2-thienylethyl	OMe	Cl	5-Cl	Me	NH2
1806	2-thienylethyl	OMe	Cl	5-Cl	Me	OH
1807	2-thienylethyl	OMe	Cl	6-Cl	H	Me
1808	2-thienylethyl	OMe	Cl	6-Cl	H	NH2
1809	2-thienylethyl	OMe	Cl	6-Cl	H	OH
1810	2-thienylethyl	OMe	Cl	6-Cl	Me	Me
1811	2-thienylethyl	OMe	Cl	6-Cl	Me	NH2
1812	2-thienylethyl	OMe	Cl	6-Cl	Me	OH
1813	2-thienylethyl	OMe	Cl	7-Cl	H	Me
1814	2-thienylethyl	OMe	Cl	7-Cl	H	NH2
1815	2-thienylethyl	OMe	Cl	7-Cl	H	OH
1816	2-thienylethyl	OMe	Cl	7-Cl	Me	Me
1817	2-thienylethyl	OMe	Cl	7-Cl	Me	NH2
1818	2-thienylethyl	OMe	Cl	7-Cl	Me	OH
1819	2-thienylethyl	OMe	Cl	5-NH2	H	Me
1820	2-thienylethyl	OMe	Cl	5-NH2	H	NH2
1821	2-thienylethyl	OMe	Cl	5-NH2	H	OH
1822	2-thienylethyl	OMe	Cl	5-NH2	Me	Me
1823	2-thienylethyl	OMe	Cl	5-NH2	Me	NH2
1824	2-thienylethyl	OMe	Cl	5-NH2	Me	OH
1825	2-thienylethyl	OMe	Cl	6-NH2	H	Me
1826	2-thienylethyl	OMe	Cl	6-NH2	H	NH2
1827	2-thienylethyl	OMe	Cl	6-NH2	H	OH
1828	2-thienylethyl	OMe	Cl	6-NH2	Me	Me
1829	2-thienylethyl	OMe	Cl	6-NH2	Me	NH2
1830	2-thienylethyl	OMe	Cl	6-NH2	Me	OH
1831	2-thienylethyl	OMe	Cl	7-NH2	H	Me
1832	2-thienylethyl	OMe	Cl	7-NH2	H	NH2
1833	2-thienylethyl	OMe	Cl	7-NH2	H	OH
1834	2-thienylethyl	OMe	Cl	7-NH2	Me	Me
1835	2-thienylethyl	OMe	Cl	7-NH2	Me	NH2
1836	2-thienylethyl	OMe	Cl	7-NH2	Me	OH
1837	2-thienylethyl	OMe	Cl	5-Me	H	Me
1838	2-thienylethyl	OMe	Cl	5-Me	H	NH2
1839	2-thienylethyl	OMe	Cl	5-Me	H	OH
1840	2-thienylethyl	OMe	Cl	5-Me	Me	Me

TABLE 47

Compound No.	R1	R2	R3	R3'	R4	R5
1841	2-thienylethyl	OMe	Cl	5-Me	Me	NH2
1842	2-thienylethyl	OMe	Cl	5-Me	Me	OH
1843	2-thienylethyl	OMe	Cl	6-Me	H	Me
1844	2-thienylethyl	OMe	Cl	6-Me	H	NH2
1845	2-thienylethyl	OMe	Cl	6-Me	H	OH
1846	2-thienylethyl	OMe	Cl	6-Me	Me	Me
1847	2-thienylethyl	OMe	Cl	6-Me	Me	NH2
1848	2-thienylethyl	OMe	Cl	6-Me	Me	OH
1849	2-thienylethyl	OMe	Cl	7-Me	H	Me
1850	2-thienylethyl	OMe	Cl	7-Me	H	NH2
1851	2-thienylethyl	OMe	Cl	7-Me	H	OH
1852	2-thienylethyl	OMe	Cl	7-Me	Me	Me
1853	2-thienylethyl	OMe	Cl	7-Me	Me	NH2
1854	2-thienylethyl	OMe	Cl	7-Me	Me	OH
1855	2-thienylethyl	OMe	NH2	5-H	H	Me
1856	2-thienylethyl	OMe	NH2	5-H	H	NH2
1857	2-thienylethyl	OMe	NH2	5-H	H	OH
1858	2-thienylethyl	OMe	NH2	5-H	Me	Me
1859	2-thienylethyl	OMe	NH2	5-H	Me	NH2
1860	2-thienylethyl	OMe	NH2	5-H	Me	OH
1861	2-thienylethyl	OMe	NH2	6-H	H	Me
1862	2-thienylethyl	OMe	NH2	6-H	H	NH2
1863	2-thienylethyl	OMe	NH2	6-H	H	OH
1864	2-thienylethyl	OMe	NH2	6-H	Me	Me
1865	2-thienylethyl	OMe	NH2	6-H	Me	NH2
1866	2-thienylethyl	OMe	NH2	6-H	Me	OH
1867	2-thienylethyl	OMe	NH2	7-H	H	Me
1868	2-thienylethyl	OMe	NH2	7-H	H	NH2
1869	2-thienylethyl	OMe	NH2	7-H	H	OH

TABLE 47-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1870	2-thienylethyl	OMe	NH2	7-H	Me	Me
1871	2-thienylethyl	OMe	NH2	7-H	Me	NH2
1872	2-thienylethyl	OMe	NH2	7-H	Me	OH
1873	2-thienylethyl	OMe	NH2	5-Cl	H	Me
1874	2-thienylethyl	OMe	NH2	5-Cl	H	NH2
1875	2-thienylethyl	OMe	NH2	5-Cl	H	OH
1876	2-thienylethyl	OMe	NH2	5-Cl	Me	Me
1877	2-thienylethyl	OMe	NH2	5-Cl	Me	NH2
1878	2-thienylethyl	OMe	NH2	5-Cl	Me	OH
1879	2-thienylethyl	OMe	NH2	6-Cl	H	Me
1880	2-thienylethyl	OMe	NH2	6-Cl	H	NH2

TABLE 48

Compound No.	R1	R2	R3	R3'	R4	R5
1881	2-thienylethyl	OMe	NH2	6-Cl	H	OH
1882	2-thienylethyl	OMe	NH2	6-Cl	Me	Me
1883	2-thienylethyl	OMe	NH2	6-Cl	Me	NH2
1884	2-thienylethyl	OMe	NH2	6-Cl	Me	OH
1885	2-thienylethyl	OMe	NH2	7-Cl	H	Me
1886	2-thienylethyl	OMe	NH2	7-Cl	H	NH2
1887	2-thienylethyl	OMe	NH2	7-Cl	H	OH
1888	2-thienylethyl	OMe	NH2	7-Cl	Me	Me
1889	2-thienylethyl	OMe	NH2	7-Cl	Me	NH2
1890	2-thienylethyl	OMe	NH2	7-Cl	Me	OH
1891	2-thienylethyl	OMe	NH2	5-NH2	H	Me
1892	2-thienylethyl	OMe	NH2	5-NH2	H	NH2
1893	2-thienylethyl	OMe	NH2	5-NH2	H	OH
1894	2-thienylethyl	OMe	NH2	5-NH2	Me	Me
1895	2-thienylethyl	OMe	NH2	5-NH2	Me	NH2
1896	2-thienylethyl	OMe	NH2	5-NH2	Me	OH
1897	2-thienylethyl	OMe	NH2	6-NH2	H	Me
1898	2-thienylethyl	OMe	NH2	6-NH2	H	NH2
1899	2-thienylethyl	OMe	NH2	6-NH2	H	OH
1900	2-thienylethyl	OMe	NH2	6-NH2	Me	Me
1901	2-thienylethyl	OMe	NH2	6-NH2	Me	NH2
1902	2-thienylethyl	OMe	NH2	6-NH2	Me	OH
1903	2-thienylethyl	OMe	NH2	7-NH2	H	Me
1904	2-thienylethyl	OMe	NH2	7-NH2	H	NH2
1905	2-thienylethyl	OMe	NH2	7-NH2	H	OH
1906	2-thienylethyl	OMe	NH2	7-NH2	Me	Me
1907	2-thienylethyl	OMe	NH2	7-NH2	Me	NH2
1908	2-thienylethyl	OMe	NH2	7-NH2	Me	OH
1909	2-thienylethyl	OMe	NH2	5-Me	H	Me
1910	2-thienylethyl	OMe	NH2	5-Me	H	NH2
1911	2-thienylethyl	OMe	NH2	5-Me	H	OH
1912	2-thienylethyl	OMe	NH2	5-Me	Me	Me
1913	2-thienylethyl	OMe	NH2	5-Me	Me	NH2
1914	2-thienylethyl	OMe	NH2	5-Me	Me	OH
1915	2-thienylethyl	OMe	NH2	6-Me	H	Me
1916	2-thienylethyl	OMe	NH2	6-Me	H	NH2
1917	2-thienylethyl	OMe	NH2	6-Me	H	OH
1918	2-thienylethyl	OMe	NH2	6-Me	Me	Me
1919	2-thienylethyl	OMe	NH2	6-Me	Me	NH2
1920	2-thienylethyl	OMe	NH2	6-Me	Me	OH

TABLE 49

Compound No.	R1	R2	R3	R3'	R4	R5
1921	2-thienylethyl	OMe	NH2	7-Me	H	Me
1922	2-thienylethyl	OMe	NH2	7-Me	H	NH2
1923	2-thienylethyl	OMe	NH2	7-Me	H	OH
1924	2-thienylethyl	OMe	NH2	7-Me	Me	Me
1925	2-thienylethyl	OMe	NH2	7-Me	Me	NH2
1926	2-thienylethyl	OMe	NH2	7-Me	Me	OH
1927	2-thienylethyl	OMe	Me	5-H	H	Me
1928	2-thienylethyl	OMe	Me	5-H	H	NH2
1929	2-thienylethyl	OMe	Me	5-H	H	OH
1930	2-thienylethyl	OMe	Me	5-H	Me	Me
1931	2-thienylethyl	OMe	Me	5-H	Me	NH2

TABLE 49-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1932	2-thienylethyl	OMe	Me	5-H	Me	OH
1933	2-thienylethyl	OMe	Me	6-H	H	Me
1934	2-thienylethyl	OMe	Me	6-H	H	NH2
1935	2-thienylethyl	OMe	Me	6-H	H	OH
1936	2-thienylethyl	OMe	Me	6-H	Me	Me
1937	2-thienylethyl	OMe	Me	6-H	Me	NH2
1938	2-thienylethyl	OMe	Me	6-H	Me	OH
1939	2-thienylethyl	OMe	Me	7-H	H	Me
1940	2-thienylethyl	OMe	Me	7-H	H	NH2
1941	2-thienylethyl	OMe	Me	7-H	H	OH
1942	2-thienylethyl	OMe	Me	7-H	Me	Me
1943	2-thienylethyl	OMe	Me	7-H	Me	NH2
1944	2-thienylethyl	OMe	Me	7-H	Me	OH
1945	2-thienylethyl	OMe	Me	5-Cl	H	Me
1946	2-thienylethyl	OMe	Me	5-Cl	H	NH2
1947	2-thienylethyl	OMe	Me	5-Cl	H	OH
1948	2-thienylethyl	OMe	Me	5-Cl	Me	Me
1949	2-thienylethyl	OMe	Me	5-Cl	Me	NH2
1950	2-thienylethyl	OMe	Me	5-Cl	Me	OH
1951	2-thienylethyl	OMe	Me	6-Cl	H	Me
1952	2-thienylethyl	OMe	Me	6-Cl	H	NH2
1953	2-thienylethyl	OMe	Me	6-Cl	H	OH
1954	2-thienylethyl	OMe	Me	6-Cl	Me	Me
1955	2-thienylethyl	OMe	Me	6-Cl	Me	NH2
1956	2-thienylethyl	OMe	Me	6-Cl	Me	OH
1957	2-thienylethyl	OMe	Me	7-Cl	H	Me
1958	2-thienylethyl	OMe	Me	7-Cl	H	NH2
1959	2-thienylethyl	OMe	Me	7-Cl	H	OH
1960	2-thienylethyl	OMe	Me	7-Cl	Me	Me

TABLE 50

Compound No.	R1	R2	R3	R3'	R4	R5
1961	2-thienylethyl	OMe	Me	7-Cl	Me	NH2
1962	2-thienylethyl	OMe	Me	7-Cl	Me	OH
1963	2-thienylethyl	OMe	Me	5-NH2	H	Me
1964	2-thienylethyl	OMe	Me	5-NH2	H	NH2
1965	2-thienylethyl	OMe	Me	5-NH2	H	OH
1966	2-thienylethyl	OMe	Me	5-NH2	Me	Me
1967	2-thienylethyl	OMe	Me	5-NH2	Me	NH2
1968	2-thienylethyl	OMe	Me	5-NH2	Me	OH
1969	2-thienylethyl	OMe	Me	6-NH2	H	Me
1970	2-thienylethyl	OMe	Me	6-NH2	H	NH2
1971	2-thienylethyl	OMe	Me	6-NH2	H	OH
1972	2-thienylethyl	OMe	Me	6-NH2	Me	Me
1973	2-thienylethyl	OMe	Me	6-NH2	Me	NH2
1974	2-thienylethyl	OMe	Me	6-NH2	Me	OH
1975	2-thienylethyl	OMe	Me	7-NH2	H	Me
1976	2-thienylethyl	OMe	Me	7-NH2	H	NH2
1977	2-thienylethyl	OMe	Me	7-NH2	H	OH
1978	2-thienylethyl	OMe	Me	7-NH2	Me	Me
1979	2-thienylethyl	OMe	Me	7-NH2	Me	NH2
1980	2-thienylethyl	OMe	Me	7-NH2	Me	OH
1981	2-thienylethyl	OMe	Me	5-Me	H	Me
1982	2-thienylethyl	OMe	Me	5-Me	H	NH2
1983	2-thienylethyl	OMe	Me	5-Me	H	OH
1984	2-thienylethyl	OMe	Me	5-Me	Me	Me
1985	2-thienylethyl	OMe	Me	5-Me	Me	NH2
1986	2-thienylethyl	OMe	Me	5-Me	Me	OH
1987	2-thienylethyl	OMe	Me	6-Me	H	Me
1988	2-thienylethyl	OMe	Me	6-Me	H	NH2
1989	2-thienylethyl	OMe	Me	6-Me	H	OH
1990	2-thienylethyl	OMe	Me	6-Me	Me	Me
1991	2-thienylethyl	OMe	Me	6-Me	Me	NH2
1992	2-thienylethyl	OMe	Me	6-Me	Me	OH
1993	2-thienylethyl	OMe	Me	7-Me	H	Me
1994	2-thienylethyl	OMe	Me	7-Me	H	NH2
1995	2-thienylethyl	OMe	Me	7-Me	H	OH
1996	2-thienylethyl	OMe	Me	7-Me	Me	Me
1997	2-thienylethyl	OMe	Me	7-Me	Me	NH2
1998	2-thienylethyl	OMe	Me	7-Me	Me	OH

TABLE 50-continued

Compound No.	R1	R2	R3	R3'	R4	R5
1999	2-thienylethyl	OMe	H	5-Cl	H	Me
2000	2-thienylethyl	OMe	H	5-Cl	H	NH2

TABLE 51

Compound No.	R1	R2	R3	R3'	R4	R5
2001	2-thienylethyl	OMe	H	5-Cl	H	OH
2002	2-thienylethyl	OMe	H	5-Cl	Me	Me
2003	2-thienylethyl	OMe	H	5-Cl	Me	NH2
2004	2-thienylethyl	OMe	H	5-Cl	Me	OH
2005	2-thienylethyl	OMe	H	6-Cl	H	Me
2006	2-thienylethyl	OMe	H	6-Cl	H	NH2
2007	2-thienylethyl	OMe	H	6-Cl	H	OH
2008	2-thienylethyl	OMe	H	6-Cl	Me	Me
2009	2-thienylethyl	OMe	H	6-Cl	Me	NH2
2010	2-thienylethyl	OMe	H	6-Cl	Me	OH
2011	2-thienylethyl	OMe	H	7-Cl	H	Me
2012	2-thienylethyl	OMe	H	7-Cl	H	NH2
2013	2-thienylethyl	OMe	H	7-Cl	H	OH
2014	2-thienylethyl	OMe	H	7-Cl	Me	Me
2015	2-thienylethyl	OMe	H	7-Cl	Me	NH2
2016	2-thienylethyl	OMe	H	7-Cl	Me	OH
2017	2-thienylethyl	OMe	H	5-NH2	H	Me
2018	2-thienylethyl	OMe	H	5-NH2	H	NH2
2019	2-thienylethyl	OMe	H	5-NH2	H	OH
2020	2-thienylethyl	OMe	H	5-NH2	Me	Me
2021	2-thienylethyl	OMe	H	5-NH2	Me	NH2
2022	2-thienylethyl	OMe	H	5-NH2	Me	OH
2023	2-thienylethyl	OMe	H	6-NH2	H	Me
2024	2-thienylethyl	OMe	H	6-NH2	H	NH2
2025	2-thienylethyl	OMe	H	6-NH2	H	OH
2026	2-thienylethyl	OMe	H	6-NH2	Me	Me
2027	2-thienylethyl	OMe	H	6-NH2	Me	NH2
2028	2-thienylethyl	OMe	H	6-NH2	Me	OH
2029	2-thienylethyl	OMe	H	7-NH2	H	Me
2030	2-thienylethyl	OMe	H	7-NH2	H	NH2
2031	2-thienylethyl	OMe	H	7-NH2	H	OH
2032	2-thienylethyl	OMe	H	7-NH2	Me	Me
2033	2-thienylethyl	OMe	H	7-NH2	Me	NH2
2034	2-thienylethyl	OMe	H	7-NH2	Me	OH
2035	2-thienylethyl	OMe	H	5-Me	H	Me
2036	2-thienylethyl	OMe	H	5-Me	H	NH2
2037	2-thienylethyl	OMe	H	5-Me	H	OH
2038	2-thienylethyl	OMe	H	5-Me	Me	Me
2039	2-thienylethyl	OMe	H	5-Me	Me	NH2
2040	2-thienylethyl	OMe	H	5-Me	Me	OH

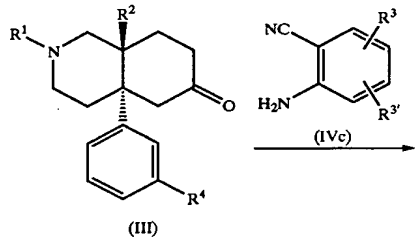
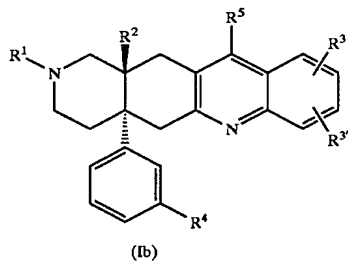
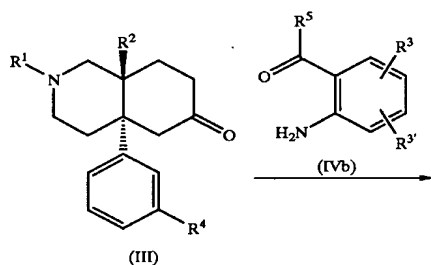
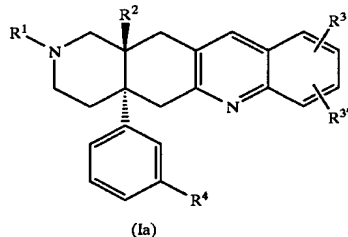
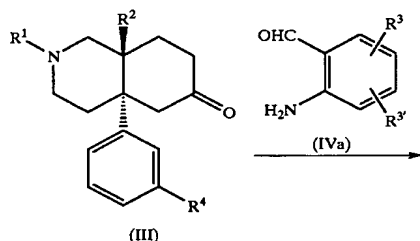
TABLE 52

Compound No.	R1	R2	R3	R3'	R4	R5
2041	2-thienylethyl	OMe	H	6-Me	H	Me
2042	2-thienylethyl	OMe	H	6-Me	H	NH2
2043	2-thienylethyl	OMe	H	6-Me	H	OH
2044	2-thienylethyl	OMe	H	6-Me	Me	Me
2045	2-thienylethyl	OMe	H	6-Me	Me	NH2
2046	2-thienylethyl	OMe	H	6-Me	Me	OH
2047	2-thienylethyl	OMe	H	7-Me	H	Me
2048	2-thienylethyl	OMe	H	7-Me	H	NH2
2049	2-thienylethyl	OMe	H	7-Me	H	OH
2050	2-thienylethyl	OMe	H	7-Me	Me	Me
2051	2-thienylethyl	OMe	H	7-Me	Me	NH2
2052	2-thienylethyl	OMe	H	7-Me	Me	OH

The compounds of Formula (I) can be obtained by, for example, condensing a ketone (III) as a starting material with o-aminobenzaldehyde derivative (IVa), o-aminoacetophenone (IVb) or o-aminobenzonitrile (IVc) in a solvent in the presence of an acid catalyst, in accordance with the method described in Japanese Laid-open Patent Application (Kokai) No. 4-275288 or WO99/02157. In this

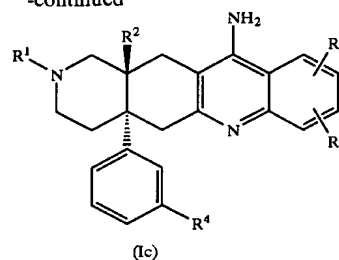
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case, by using an optically active compound as the starting material, an optically active compound can be obtained (Scheme 1).



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-continued



The fact that the isoquinoline derivatives of Formula (I) are effective for therapy and/or prevention of memory disorder may be confirmed by a behavioral pharmacological method using animals as described in Examples. More specifically, the passive avoidance test, the conditioned active avoidance test, or the spacial memory test using a water maize or a radial type maze are often used to develop an anti-dementia drug.

The compounds of the present invention may be used as pharmaceuticals useful for therapy and/or prevention of dementia accompanying learning disability and/or memory disorder. Especially, they may be used for therapy and/or prevention of dementia accompanying memory disorder caused by a cerebrovascular disease, neurodegenerative disease, endocrine disease, nutritional or metabolic disorder, anoxic encephalopathy, tumor, infectious disease, disorder of metabolism of a metal, or drug addiction. Examples of cerebrovascular diseases exhibiting dementia include cerebral infarction, cerebral hemorrhage, multiinfarct dementia, moyamoya disease, intracranial arteriovenous malformation, systemic lupus erythematosus (SLE) and angitis such as temporal arteritis. Examples of neurodegenerative diseases accompanying dementia include Alzheimer's disease, Pick's disease, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, Shy-Drager syndrome, Ramsay Hunt's syndrome and familial basal ganglia calcification. Examples of endocrine diseases include hypothyroidism, hypoparathyroidism syndrome, Cushing's disease, Addison's disease and recurrent hypoglycemic attack. Examples of nutritional or metabolic disorder include Wernicke encephalitis, pellagra encephalopathy, vitamin B12 deficiency, chronic metabolic disorders such as hepatic insufficiency and renal insufficiency, and hyponatremia. Examples of anoxic encephalopathy include carbon monoxide poisoning. Examples of tumors include cerebral tumor and meningitis carcinomatosa. Examples of infectious diseases include cerebral meningitis, encephalitis, cerebral tumor, slow virus disease, AIDS and neurosyphilis. Examples of other diseases which exhibit dementia include normal pressure hydrocephalus, chronic subdural hematoma, brain contusion, myotonic dystrophy and mitochondrial myopathy. The application of the compounds of the present invention is not restricted to these diseases.

The agent for improving learning and/or memory according to the present invention may be used in combination with one or more of other drugs for therapy and/or prevention of diseases exhibiting dementia (e.g., cerebrovascular diseases, neurodegenerative diseases, endocrine diseases, nutritional or metabolic disorder, anoxic encephalopathy, malignant tumors and infectious diseases) and drugs used for problematic behavior accompanied by dementia (night delirium, night restlessness, depression, sleep disorder and personality change).

Examples of the drugs for prevention and/or therapy of cerebrovascular diseases include cerebral circulation metabolism activators such as ATP, cytochrome c, meclofenoxate hydrochloride, idebenone, propentofylline, γ -aminobutyric acid, γ -amino- β -hydroxybutyric acid, cal-

cium hopantenate, anirasetam, amantadine hydrochloride, lisuride maleate, bifemelane hydrochloride, indeloxazine hydrochloride, dihydroergotamine mesylate, ifenprodil tartrate, moxislyte hydrochloride, bencylamine fumarate, brovincamine fumarate, ibudilast, vinpocetine, nicergoline, cinapazide maleate, pentoxifylline, trapidil, dilazep hydrochloride, flunarizine hydrochloride, cinnarizine, nicaldipine hydrochloride, nilvadipine and kallidinogenase; antihypertensive drugs such as chlorothiazide, ethacrynic acid, clonidine, reserpine, propranolol, prazosin, hydralazine, papaverine, captopril and nifedipine; anticoagulant drugs such as warfarin; thrombolytic agents such as urokinase; anti-platelet agents such as ozagrel and beraprost.

Examples of drugs for prevention and/or therapy of neurodegenerative diseases include anti-dementia drugs such as tacrine, therapeutic agents for Parkinson's disease such as levodopa, benserazide, deprenyl, biperiden, promethazine and diphenhydramine, as well as the above-mentioned cerebral circulation metabolism activators.

Examples of the drugs for prevention and/or therapy of problematic behavior accompanied by dementia include antidepressant drugs such as amitriptyline, dothiepin, lofepramine, imipramine, fluoxetine, fluvoxamine, mianserin, trazodone, maprotiline and safrazine; anti-anxiety agents such as diazepam and meprobamate; hypnotics such as haloxazolam and triazolam; and neuroplegics such as chlorpromazine, thioridazine and fluphenazine.

Examples of the drugs for prevention and/or therapy of endocrine diseases include antithyroid drugs (e.g., thionamide, methimazole and iodine), antidiabetic drugs (e.g., insulin formulation, tolbutamide, glipizide, metformin and acarbose), adrenocorticotrophic hormones (e.g., glucocorticoids such as hydrocortisone, prednisolone, betamethasone, dexamethasone; and mineral corticoids such as aldosterone), and anti-adrenocorticotrophic hormones (e.g., metyrapone).

Examples of the drugs for prevention and/or therapy of malignant tumors include alkylating agents such as cyclophosphamide and chlorambucil; cytotoxic antibiotics such as doxorubicin; vinca alkaloids such as vincristine; antimitotics such as methotrexate, fluorouracil, cytarabine and mercaptopurine; and cisplatin.

When the agent for improving learning and/or memory according to the present invention is clinically used, the agent may be in the form of free base or salt thereof per se, or may be admixed with one or more additives such as vehicles, stabilizers, preservatives, buffer agents, solubilizers, emulsifiers, diluents and isotonic agents. The agent may be administered either orally or parenterally. The agent may be formulated in the form of injection solution, tablets, solution, capsules, granules, powder or the like. These formulations may be produced by known formulation techniques. The dose may be appropriately selected depending on the symptoms, age and bodyweight of the patient, and administration route. The dose of the effective component for an adult may be 0.0001 mg to 10 g per day, preferably 0.001 mg to 1 g per day, and the agent may be administered in one time or in several times.

EXAMPLES

The present invention will now be described concretely referring to Reference Examples and Examples.

Reference Example 1

(4aR, 12aR)-2-methyl-4a-(3-hydroxyphenyl)-1,2,3,4,4a,5,12,12a-octahydro-quinolino[2,3-g]isoquinoline 1 Methanesulfonic Acid Salt

This compound was synthesized by the method described in WO99/02157.

Reference Example 2

2-methyl-4a-(3-methoxyphenyl)-11-methyl-1,2,3,4,4a,5,12,12a β -octahydro-quinolino[2,3-g]isoquinoline 2

To 5 mL of acetic acid, 150 mg (0.55 mmol) of 2-methyl-4a-(3-methoxyphenyl)-6-oxo-1,2,3,4,4a,5,6,7,8,8a β -octahydroisoquinoline and 100 mg (0.74 mmol) of o-aminoacetophenone were added and the mixture was heated to reflux for 3 hours. After allowing the mixture to cool, saturated aqueous sodium hydrogen carbonate solution was added and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The obtained residue was subjected to silica gel column chromatography (chloroform:methanol:28% aqueous ammonia=20:1:0.1 to 10:1:0.1) for purification to obtain 211 mg of the captioned compound (yield: 100%).

Reference Example 3

2-methyl-4a-(3-hydroxyphenyl)-11-methyl-1,2,3,4,4a,5,12,12a β -octahydro-quinolino[2,3-g]isoquinoline 3 Hydrochloric Acid Salt

In 7 mL of DMF solvent, 210 mg (0.56 mmol) of 2-methyl-4a-(3-methoxyphenyl)-11-methyl-1,2,3,4,4a,5,12,12a β -octahydro-quinolino[2,3-g]isoquinoline obtained in Reference Example 2 and 0.29 mL (3.20 mmol) of n-propanethiol were dissolved under argon atmosphere. To the mixture, 320 mg (2.85 mmol) of potassium-t-butoxide was added and the mixture was heated at 120° C. for 20 hours under stirring. To the mixture, 4 mL of 1N hydrochloric acid was added while cooling the mixture in ice to make the mixture acidic, and then saturated aqueous sodium hydrogen carbonate solution was added to make the mixture again basic, followed by extraction of the resulting mixture with chloroform:methanol (4:1) mixture. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration of the resulting product. The obtained residue was recrystallized from dichloromethane-methanol mixture to obtain 131 mg of the captioned compound (yield: 65%). The obtained product was suspended in methanol and hydrochloric acid was added to convert the compound to a salt. After concentration of the product, ether was added and solids were collected by filtration to obtain 143 mg of hydrochloric acid salt of the captioned compound.

Reference Example 4

2-methyl-4a-(3-methoxyphenyl)-11-amino-1,2,3,4,4a,5,12,12a β -octahydro-quinolino[2,3-g]isoquinoline 4

To 5 mL of acetic acid, 150 mg (0.55 mmol) of 2-methyl-4a-(3-methoxyphenyl)-6-oxo-1,2,3,4,4a,5,6,7,8,8a β -octahydroisoquinoline and 130 mg (1.10 mmol) of o-aminobenzonitrile were added, and the mixture was heated to reflux for 44 hours. After allowing the mixture to cool, saturated aqueous sodium hydrogen carbonate solution was added, and the resulting mixture was extracted with chloroform:methanol (4:1) mixture. The organic layer was washed with brine and dried over anhydrous magnesium sulfate, followed by concentration of the obtained product. The obtained residue was subjected to amine-coated silica gel column chromatography (chloroform:methanol=50:1) for purification to obtain 83 mg of the captioned compound (yield: 41%).

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Reference Example 5

2-methyl-4a-(3-hydroxyphenyl)-11-amino-1,2,3,4,
4a,5,12,12a β -octahydro-quinolino[2,3-g]
isoquinoline 5 Hydrochloric Acid Salt

In 7 mL of DMF solvent, 83 mg (0.22 mmol) of 2-methyl-4a-(3-methoxyphenyl)-11-amino-1,2,3,4,4a,5,12,12a β -octahydro-quinolino[2,3-g]isoquinoline obtained in Reference Example 4 and 0.10 mL (1.060 mmol) of n-propanethiol were dissolved under argon atmosphere. To the mixture, 106 mg (0.95 mmol) of potassium-t-butoxide was added and the mixture was heated at 120° C. for 20 hours under stirring. To the mixture, 4 mL of 1N hydrochloric acid was added while cooling the mixture in ice to make the mixture acidic, and then saturated aqueous sodium hydrogen carbonate solution was added to make the mixture again basic, followed by extraction of the resulting mixture with chloroform:methanol (4:1) mixture. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration of the resulting product. The obtained residue was recrystallized from dichloromethane-methanol mixture to obtain 35 mg of the captioned compound (yield: 44%). The obtained product was suspended in methanol and hydrochloric acid was added to convert the compound to a salt. After concentration of the product, ether was added and solids were collected by filtration to obtain 40 mg of hydrochloric acid salt of the captioned compound.

Reference Example 6

(+)-7,9-dibromo-4a-(3-methoxyphenyl)-2-methyl-1,
2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]
isoquinoline 6

In ethanol, 382.4 mg of (+)-4a-(3-methoxyphenyl)-2-methyl-6-oxo-1,2,3,4,4a,5,6,7,8,8a-octahydroisoquinoline and 1.95 g of 2-amino-3,5-dibromobenzaldehyde were dissolved, and 0.454 mL of methanesulfonic acid was added, followed by heating the resulting mixture to reflux for 2 hours. After allowing the mixture to cool, saturated aqueous sodium hydrogen carbonate solution was added and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After filtration and concentration, the obtained residue was purified by silica gel column chromatography (chloroform:methanol=40:1) to obtain 683.7 mg of the captioned compound (yield: 95%).

Reference Example 7

(+)-7,9-dibromo-4a-(3-hydroxyphenyl)-2-methyl-1,
2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]
isoquinoline 7

In 15 mL of dichloromethane, 669.6 mg of (+)-7,9-dibromo-4a-(3-methoxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline obtained in Reference Example 6 was dissolved, and 6.49 mL of boron tribromide solution in dichloromethane (1 mol/L) was added dropwise while cooling the mixture in ice. After stirring the mixture at 0° C. for 4 hours, saturated aqueous sodium hydrogen carbonate solution was added and the resulting mixture was vigorously stirred for 30 minutes at room temperature. After extracting the mixture with chloroform, the organic layer was washed with brine and dried over anhydrous sodium sulfate. After filtration and concentration, the obtained residue was purified by silica gel column

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chromatography (chloroform:methanol=20:1-5:1) to obtain 381.5 mg of the captioned compound (yield: 59%).

Reference Example 8

(+)-7,9-dibromo-4a-(3-hydroxyphenyl)-2-methyl-1,
2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]
isoquinoline Methanesulfonic Acid Salt 8

In methanol, 381.5 mg of (+)-7,9-dibromo-4a-(3-hydroxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline obtained in Reference Example 7 was suspended, and 1.522 mL of methanesulfonic acid was added, followed by stirring the mixture for 10 minutes. The reaction solution was concentrated and the obtained residue was reprecipitated from methanol, ethyl acetate and diethyl-ether to obtain 348.2 mg of the captioned compound.

Reference Example 9

(+)-9-fluoro-4a-(3-methoxyphenyl)-2-methyl-1,2,3,
4,4a,5,12,12a-octahydro-quinoline[2,3 g]
isoquinoline 9

A mixture of 380.3 mg of (+)-4a-(3-methoxyphenyl)-2-methyl-6-oxo-1,2,3,4,4a,5,6,7,8,8a-octahydroisoquinoline and 0.924 mL of dimethylformamide dimethylacetal in toluene solvent was heated to reflux for 5.5 hours. After allowing the mixture to cool, the reaction solution was concentrated and dried under reduced pressure. The residue was dissolved in 8 mL of xylene, and 0.395 mL of 4-fluoroaniline and 0.536 mL of trifluoroacetic acid were added, followed by heating the resulting mixture to reflux for 11 hours. After allowing the mixture to cool, saturated aqueous sodium hydrogen carbonate solution was added and the mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous sodium sulfate. After filtration and concentration, the obtained residue was purified by silica gel column chromatography (chloroform:methanol=15:1-10:1) to obtain 249.9 mg of the captioned compound (yield: 48%).

Reference Example 10

(+)-9-fluoro-4a-(3-hydroxyphenyl)-2-methyl-1,2,3,4,
4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline
10

In 9 mL of dichloromethane, 249.9 mg of (+)-9-fluoro-4a-(3-methoxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline obtained in Reference Example 9 was dissolved, and 3.32 mL of 1N boron tribromide solution in dichloromethane was added dropwise while cooling the mixture in ice, and then the resulting mixture was stirred for 2 hours. Saturated aqueous sodium hydrogen carbonate solution was slowly added and the mixture was vigorously stirred for 30 minutes. The reaction solution was extracted with chloroform and the organic layer was washed with brine, followed by drying over anhydrous sodium sulfate. After filtration and concentration, the obtained residue was purified by silica gel column chromatography (chloroform:methanol:isopropylamine=97:2.7:0.3), and then by thin layer chromatography (chloroform:chloroform saturated with ammonia=1:1) to obtain 65 mg of the captioned compound (yield: 27%).

Reference Example 11

(+)-9-fluoro-4a-(3-hydroxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline
Tartaric Acid Salt 11

In 2 ml of methanol, 48.6 mg of (+)-9-fluoro-4a-(3-hydroxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-quinoline[2,3 g]isoquinoline obtained in Reference Example

10 was dissolved, and 40.2 mg of L-tartaric acid was added, followed by stirring the mixture for 10 minutes. After concentrating the reaction solution, the residue was reprecipitated from methanol-ethyl acetate mixed solvent to obtain 57.0 mg of the captioned compound.

The chemical structure, acid addition salts and various spectra data of the Compounds 2 to 11 described in the Reference Examples are shown in Tables 53 to 56 below.

TABLE 53

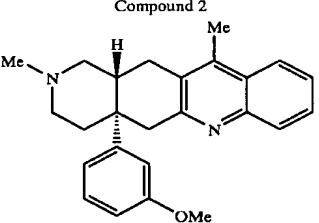
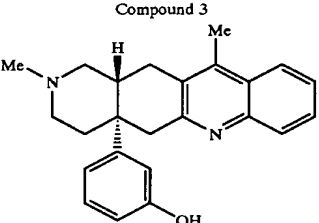
Yield (%)	NMR (ppm) (300 MHz CDCl ₃)	m.p. (° C.)
Compound 2	2.0(1H, m), 2.16(1H, m), 2.3(1H, m), 2.41(3H, s), 2.51(3H, s), 2.7(2H, m), 2.82(1H, t, J=11.5Hz), 3.06(3H, m), 3.14(1H, d, J=16.5Hz), 3.68(3H, s), 3.74(1H, d, J=16.5Hz), 6.67(1H, m), 7.06(1H, m), 7.42(1H, m), 7.55(1H, m), 7.9(2H, m)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) (KBr) 2928, 2798, 1607, 1582, 1487, 1431, 1288, 1230 Mass (EI) 372 (M+) (data of salt-free compound)
		
Yield (%)	NMR (ppm) (500 MHz, D ₂ O)	m.p. (° C.)
Compound 3	2.27(1H, dt, J=14.5, 3.4Hz), 2.68(1H, t, J=11.7Hz), 2.81(3H, s), 2.97(1H, m), 3.3(2H, m), 3.4-3.6(4H, m), 3.68(1H, dd, J=12.7, 3.2Hz), 3.95(1H, d, J=17.0Hz), 6.54(1H, dd, J=8.1, 2.0Hz), 6.95(1H, d, J=7.9Hz), 7.01(1H, m), 7.06(1H, t, J=8.1Hz), 7.83(1H, t, J=7.7Hz), 7.99(1H, t, J=7.7Hz), 8.22(1H, d, J=8.5Hz), 8.39(1H, d, J=8.7Hz)	Elementary Analysis Composition Formula C ₂₄ H ₂₆ N ₂ O/2HCl/0.6H ₂ O Calcd. C: 65.19, H: 6.66, N: 6.33, Cl: 16.03 Found C: 65.05, H: 6.90, N: 6.31, Cl: 16.13 IR (cm ⁻¹) Mass (EI) 358 (M+)
		

TABLE 54

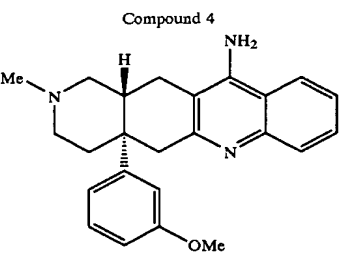
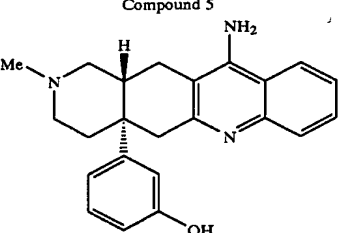
Yield (%)	NMR (ppm) (300 MHz, CDCl ₃)	m.p. (° C.)
Compound 4	2.0(1H, m), 2.1(1H, m), 2.28(1H, m), 2.38(3H, s), 2.6-2.9(5H, m), 2.97(1H, dd, J=11.0, 3.3Hz), 3.05(1H, d, J=16.5Hz), 3.64(1H, d, J=16.8Hz), 3.67(3H, s), 4.58(2H, brs), 6.58(1H, m), 7.05(3H, m), 7.32(1H, dt, J=7.5, 1.2Hz), 7.51(1H, dt, J=7.5, 1.2Hz), 7.61(1H, dd, J=8.5, 0.5Hz), 7.82(1H, dd, J=8.5, 0.5Hz)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) (KBr) 3058, 2918, 2800, 1651, 1578, 1502, 1439, 1243 Mass (EI) 373 (M+)
		
Yield (%)	NMR (ppm) (500 MHz, D ₂ O)	m.p. (° C.)
Compound 5	2.21(1H, dt, J=14.5, 2.5Hz), 2.49(1H, d, J=12.5Hz), 2.67(1H, t, J=12.7Hz), 2.84(3H, s), 2.8-2.9(3H, m), 3.17(1H, d, J=16.9Hz), 3.4-3.5(3H, m), 3.60(1H, d, J=10.3Hz), 6.58(2H, m), 6.90(2H, m), 7.09(1H, t, J=8.1Hz), 7.61(1H, d, J=7.3, 1.6Hz), 7.86(2H, m), 8.47(1H, d, J=8.5Hz)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) Mass (EI) 359 (M+)
		

TABLE 55

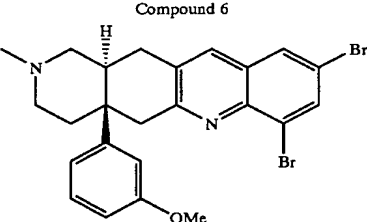
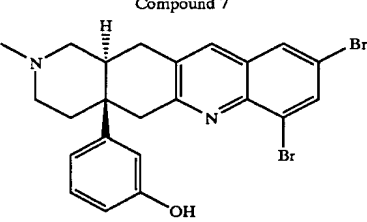
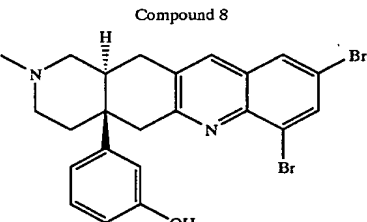
	NMR (ppm) (300 MHz, CDCl ₃)	m.p. (° C.)
<p>Compound 6</p> 	2.03–2.09(1H, m), 2.17–2.31(2H, m), 2.40(3H, s), 2.62–2.72(2H, m), 2.78(1H, t, J=11.5Hz), 3.00(1H, dd, J=2.7, 11.0Hz), 3.08–3.30(3H, m), 3.67(3H, s), 3.83(1H, d, J=16.8Hz), 6.57–6.60(1H, m), 7.03(1H, s), 7.05(1H, s), 7.09(1H, t, J=8.5Hz), 7.58–7.72(2H, brn), 7.92(1H, s)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) Mass
<p>Compound 7</p> 	2.14(1H, dt, J = 3.6, 14.3Hz), 2.30(1H, d, J=14.6Hz), 2.43(1H, brt, J=11.8Hz), 2.52(3H, s), 2.75–2.84(1H, m), 2.96–3.21(6H, m), 3.76(1H, d, J=17.0Hz), 6.48(1H, td, J=1.6, 8.0Hz), 6.81–6.86(2H, m), 6.93(1H, t, J=7.7Hz), 7.59(1H, s), 7.66(1H, d, J=2.2Hz), 7.89(1H, t, J=1.1Hz)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) Mass (EI) LR ((M + 2)+)502
	NMR (ppm) (300 MHz, CD ₃ OD)	m.p. (° C.)
<p>Compound 8</p>  <p>dimethanesulfonic acid salt</p>	2.26–2.30(1H, br), 2.66–2.71(1H, br), 2.71(6H, s), 2.85(1H, t, J=12.6Hz), 2.96(3H, s), 3.38(1H, brd, J=17.3Hz), 3.48–3.58(3H, brn), 3.66(1H, brt, J=12.9Hz), 3.77(1H, brd, J=12.6Hz), 4.23(1H, brd, J=17.9Hz), 6.59(1H, d, J=8.0Hz), 6.98(1H, brs), 7.03(1H, brd, J=7.7Hz), 7.12(1H, t, J=7.7Hz), 8.18(1H, brs), 8.24(1H, brs), 8.54(1H, brs)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) (neat) 3425, 2529, 1638, 1447 Mass

TABLE 56

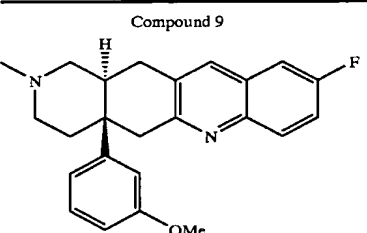
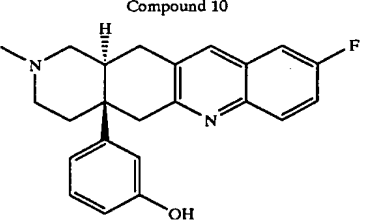
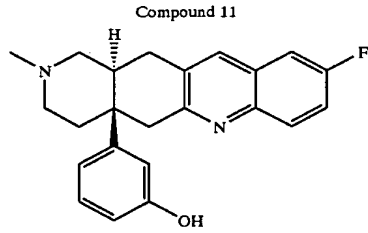
	NMR (ppm) (300 MHz, CDCl ₃)	m.p. (° C.)
<p>Compound 9</p> 	1.96(1H, dt, J=3.3, 12.6Hz), 2.10(1H, dt, J=1.9, 12.4Hz), 2.23(1H, d, J=11.5Hz), 2.33(3H, s), 2.52–2.74(3H, m), 2.90(1H, dd, J=3.8, 11.0Hz), 3.02–3.26(3H, m), 3.63(3H, d, J=0.8Hz), 3.68(1H, d, J=16.5Hz), 6.51–6.57(1H, m), 7.01–7.07(3H, m), 7.16(1H, dd, J=2.7, 9.1Hz), 7.27(1H, dd, J=3.0, 8.5Hz), 7.63(1H, s), 7.83(1H, dd, J=5.5, 9.3Hz)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) Mass
<p>Compound 10</p> 	1.91–2.00(1H, br), 2.16–2.22(2H, brn), 2.35(3H, s), 2.57–2.65(1H, brn), 2.73(1H, d, J=11.5Hz), 2.85(1H, t, J=11.8Hz), 2.93–3.19(4H, m), 3.58(1H, d, J=16.5Hz), 6.41–6.46(1H, m), 6.82–6.91(3H, m), 7.15(1H, dd, J=2.7, 9.1Hz), 7.20–7.28(1H, m), 7.66(1H, s), 7.73(1H, dd, J=5.2, 9.1Hz)	Elementary Analysis Composition Formula Calcd. Found IR (cm ⁻¹) Mass (EI) LR (M+) ⁺ 362
	NMR (ppm) (300 MHz, CD ₃ OD)	m.p. (° C.)

TABLE 56-continued

<p>Compound 11</p>  <p>ditartaric acid salt</p>	<p>2.28–2.33(1H, br), 2.52(1H, brd, J=14.8Hz), 2.79–2.88(2H, brm), 2.88(3H, s), 3.17(1H, brd, J=16.2Hz), 3.29–3.69(6H, brm), 4.48(4H, s), 6.53(1H, d, J=6.9Hz), 6.92(1H, s), 6.93(1H, d, J=6.9Hz), 7.04(1H, t, J=8.0Hz), 7.36–7.42(2H, br), 7.81–7.85(1H, br), 7.90–7.94(1H, br)</p>	<p>Elementary Analysis Composition Formula Calcd. Found IR (cm⁻¹) Mass</p>
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Example 1

Evaluation of Activity to Improve Learning and/or Memory Using Morris Water Maze
<Experiment Schedule>

In experiments, ICR male mice of 6 weeks old were used. Using Morris water maze as an experiment apparatus, ability of learning and memory of space was evaluated based on the latency until a mouse escapes to a platform arranged in a pool as an index. One trial was maximally 120 seconds, and 1 session was composed of three trials in which each mouse was made to swim in the pool from three different positions. Average time needed for the escape was calculated and evaluation was made based thereon. On the first day (the first session), no drug and nothing were administered. From the second session (Day 2), Compound 1, Compound 8 or a solvent was administered. Trial was repeated for 5 days (5 sessions).

The dose of Compound 1 was 10, 30 or 100 $\mu\text{g/kg}$, and the dose of Compound 8 was 100 $\mu\text{g/kg}$. Compound 1, Compound 8 or saline which was the solvent was subcutaneously administered 30 minutes before the first trial of each session. The data was subjected to analysis of variance and significance was evaluated according to Fisher's PLSD test. The cases where $P<0.05$ was evaluated as significant.

<Evaluation of Compound 1>

No difference in the time period required for escaping to the platform between the groups was observed in Session 1. With proceeding of the sessions, the time period required for the escaping to the platform was shortened in the group to which physiological saline was administered. On the other hand, as shown in FIG. 1, by administration of Compound 1, the time period required for the escaping to the platform was shortened dose-dependently from the second session, so that clear improvement in the ability of learning and memory of space was observed.

FIG. 1 shows the comparison between the learning process of the rats to which Compound 1 was administered and that of the rats to which saline was administered. In the graph, the ordinate indicates latency for reaching the platform (and SE), and abscissa indicates the number of sessions (* means $P<0.05$, and ** means $P<0.01$). It was shown that ability of learning and memory of space was improved in the Morris water maze test by administration of Compound 1.

<Evaluation of Compound 8>

Similar to the evaluation of Compound 1, the latency required for escaping to the platform by mice was shortened by administration of Compound 8, and clear improvement in the ability of learning and memory of space was observed. FIG. 3 shows the comparison between the learning process of the rats to which Compound 8 was administered and that of the rats to which saline was administered.

Example 2

Effect for Improvement of Learning in Test of Learning of Step-Down Type Passive Avoidance
<Experiment Schedule>

In experiments, ICR male mice of 6 weeks old were used. The experiment apparatus comprised a plastic box sizing 25×25×30 cm (width×depth×height), a stainless steel grid for giving electrical shock, which was laid on the floor of the box, and a wooden platform sizing 4.5×4.5×3.0 cm (width×depth×height) placed on a corner on the floor grid.

Sixty minutes before the training trial, 100 or 300 $\mu\text{g/kg}$ of Compound 1, or its solvent, saline, was subcutaneously administered. Thirty minutes later, 0.1 mg/kg of MK-801 which is a non-competitive antagonist of NMDA receptor, which is a compound that causes learning disability and/or memory disorder was intraperitoneally administered. Training trial was carried out by placing a mouse on the platform, and the time period until the mouse stepped down to the floor grid, that is, the Step-Down latency, was measured. Simultaneously with the attaching all of the feet of the mouse to the floor, an electrical shock of 0.6 mA was given for 2 seconds, thereby making the mouse to learn that an electrical shock would be given if the mouse would stepped down to the floor. Only the mice which showed the Step-Down latency of 3 to 30 seconds in the training trials were used in the test trials.

Test trials were carried out 24 hours after the training trials. Each mouse was again placed on the platform, and the Step-Down latency was measured for maximally 300 seconds.

<Evaluation of Compound 1>

The results are shown in FIG. 2. In the control group to which the solvent alone was administered, the Step-Down latency in the test trials was extended than that in the training trials, so that it was shown that the mice memorized that electrical shock was given when they stepped down to the floor. On the other hand, in the group to which MK-801 alone was administered, the Step-Down latency was significantly shorter than that of the control group, so that learning disability and memory disorder were induced. The action of shortening the Step-Down latency by MK-801 was significantly reduced by administration of Compound 1, so that it was observed that Compound 1 exhibited activity to improve the learning disability and memory disorder induced by MK-801.

FIG. 2 shows the Step-Down latency of the control group to which solvent alone was administered, the groups to which MK-801 was administered and of the groups to which Compound 1 was administered (the bar in each column is the median). In the group to which MK-801 was administered, the passive avoidance reaction was significantly suppressed

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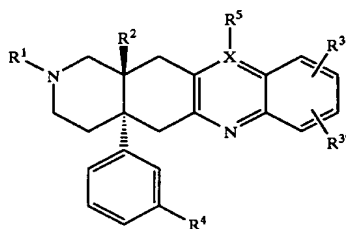
when compared with the control group. This suppressant was recovered by administration of Compound 1, so that it was shown that Compound 1 had an activity to improve the learning disability and memory disorder induced by MK-801 (** means $P < 0.01$ vs. the control, and ## means $P < 0.01$ vs. the group to which MK-801 alone was administered).

Industrial Availability

The agent for improving learning and/or memory according to the present invention is useful for the therapy of dementia accompanying disorder of memory due to a cerebrovascular disease, neurodegenerative disease such as Alzheimer's disease, endocrine disease, nutritional or metabolic disorder, infectious disease, drug addiction or the like.

What is claimed is:

1. A method for improving learning and/or memory in a subject which comprises administering to the subject an effective amount of an isoquinoline



derivative of the Formula (I):

wherein R^1 represents hydrogen, C_1-C_5 alkyl, C_4-C_7 cycloalkylalkyl, C_5-C_7 cycloalkenylalkyl, C_7-C_{14}

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aralkyl, C_4-C_5 transalkenyl, allyl, furanyl-2-ylalkyl, thienyl-2-ylalkyl, C_1-C_5 alkanoyl, benzoyl, vinyloxycarbonyl, trichloroethoxycarbonyl, benzyloxycarbonyl or C_8-C_{14} arylalkanoyl; R^2 represents hydrogen or OR^6 (wherein R^6 represents hydrogen, C_1-C_5 alkyl or C_1-C_5 alkanoyl); R^3 and R^3' independently represent C_1-C_5 alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C_1-C_3 alkoxy, C_1-C_3 alkylcarbonylamino, C_1-C_5 alkoxy, nitro, amino, or C_1-C_3 alkylamino; R^4 represents hydrogen, hydroxy, C_1-C_3 alkoxy, benzyl, or C_1-C_5 alkanoyl or halogen; X represents nitrogen or carbon; R^5 exists only when X is carbon, and represents C_1-C_5 alkyl, hydrogen, chlorine, fluorine, bromine, iodine, trifluoromethyl, cyano, hydroxy, C_1-C_3 alkoxy, C_1-C_3 alkylcarbonylamino, C_1-C_5 alkoxy, nitro, amino or C_1-C_3 alkylamino or a pharmaceutically acceptable salt thereof.

2. The method for improving learning and/or memory according to claim 1, wherein in Formula (I), R^1 is hydrogen, methyl, ethyl, cyclopropylmethyl, allyl, phenethyl, furan-2-ylethyl or thiophene-2-ylethyl; R^2 is hydrogen, hydroxy, methoxy or ethoxy; R^3 and R^3' independently are methyl, hydrogen, chlorine, fluorine, bromine, iodine, hydroxy, methoxy, nitro, amino or dimethylamino; R^4 is hydrogen, hydroxy or methoxy; X is carbon; R^5 is methyl, hydrogen, chlorine, fluorine, bromine, iodine, hydroxy, methoxy, nitro, amino or dimethylamino.

* * * * *